Splitting tablets

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SYNOPSIS

Patients split tablets for a variety of reasons, however there are problems associated with this process. Tablet-related factors include inaccuracy in splitting tablets and the resultant dose fluctuations, increased degradation of drug as a result of exposure to air and alterations in the dissolution rate of some formulations. Even when commercial tablet cutters are used the accuracy of splitting may be variable. Patients may experience difficulty in splitting tablets especially if their dexterity, eyesight or cognition is impaired. Compliance is likely to be decreased if the regimen requires tablets to be split. Although splitting tablets may potentially save the patient money the possible impact on the quality of medication use must be considered.

Index words: compliance, dosing, quality use of medicines.

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Introduction

Tablet splitting or dividing has been an accepted practice for many years as a means of obtaining the prescribed dose of a medication. Patients may be required to split tablets to:

- obtain the required dosage when a dosage form of the required strength is unavailable
- provide appropriate fractional doses in a flexible dosing regimen or in a gradually increasing or decreasing dosage regimen
- begin therapy with the lowest possible dose to decrease the incidence of adverse effects or to gauge an individual patient's response.

Elderly people or children who require reduced doses may not be able to use liquid formulations (or they may not be available on the Pharmaceutical Benefits Scheme). If suitable low-dose tablet formulations are unavailable, these patients may require tablets to be split to obtain the appropriate dosage.

Patients may save money if there is a price differential that makes halving tablets economically attractive. However, the process of splitting tablets causes a number of problems, some of which are patient-related while others are related to the tablet or formulation.

Tablet or formulation-related factors

Uneven breaking of a tablet may result in significant fluctuations in the administered dose. This may be clinically significant for drugs with a narrow therapeutic range[1], such as warfarin or digoxin. For many drugs, however, especially those with long half-lives and/or a wide therapeutic range, dose fluctuations are unlikely to be clinically significant.

Removing tablets from foil packaging or exposing uncoated tablet surfaces may increase the rate of degradation of the active drug. This has important ramifications as the patient may get a lower than intended dose and adverse effects may be increased by degradation products. The tablet dissolution rate and absorption characteristics may also be affected when tablets are split.[2] This applies particularly to coated and controlled-release tablets. While the cumulative dissolution may be similar between whole and halved tablets the initial rate of dissolution may be increased with unpredictable clinical consequences. Some sustained-release (extended duration) formulations can be halved without affecting their extended-release characteristics (e.g. isosorbide mononitrate, bupropion) while others cannot (e.g. felodipine (Agon SR), tramadol (Tramal SR)) and it is therefore important to check the product information of each specific brand if splitting tablets is considered. Many tablets are coated to mask the taste of the drug. Splitting may therefore expose a drug's taste. Table 1 provides a general guide, with limited examples, as to which tablets may not be suitable for splitting.

Tablets that are scored are usually considered by the manufacturer to be suitable for division and the majority of tablets are made this way. Not all tablets, however, are suitable

Table 1

Types of tablets that are not recommended to be split

Types of tablets that should not be split	*Examples (not a complete list)*
Unscored tablets	d-penicillamine (D-Penamine) acarbose (Glucobay 50 mg) metformin (Diaformin 850) tiludronate (Skelid)
Unusually thick or oddly shaped tablets	alendronate 40 mg (Fosamax 40 mg) finasteride (Proscar 5 mg) fosinapril (Monopril) amiloride (Midamor)
Film-coated tablets	nifedipine (Nifecard) donepezil (Aricept) tamoxifen (Nolvadex) azathioprine (Imuran 25 mg)
Enteric-coated tablets	valproate (Epilim 200 mg, Epilim 500 mg) diclofenac (Voltaren) mesalazine (Mesasal) pantoprazole (Somac)
Some time-release and extended-release tablets	felodipine (Agon SR) cefaclor CD 375 mg (all brands) potassium chloride (KSR, Slow K, Span K) tramadol (Tramal SR)

Table 2

Factors contributing to increased inaccuracy of tablet splitting

Tablet factor contributing to inaccuracy	*Examples (not a complete list)*
Small size	digoxin (Lanoxin-PG) temazepam (Temaze)
Irregular shape	fosinapril (Monopril) lamotrigine (Lamictal) alendronate (Fosamax) auranofin (Ridaura)
Scored on one side only	alprazolam (Kalma) benztropine (Cogentin) selegiline (Eldepryl) clozapine (Clozaril)

for splitting and this should be considered when the recommendation to split the tablet is made. The degree of inaccuracy may be associated with tablet size, shape and type of scoring (Table 2). Some tablets, even with a score line, may not break easily into two pieces of equal size.[1] The length of time that drugs remain stable after splitting also needs to be considered as the drug may not be stable when the cut surface is exposed to air for even short periods (up to 24 hours) let alone tablets pre-cut for doses a week or more in advance. This may be of importance if a carer, district nurse or pharmacist has to split tablets in advance for patients unable to manage the task.

The storage of split tablets is not well discussed in the literature. Anecdotal evidence suggests that many patients, or their carer, nurse or pharmacist, split a number of tablets in advance. Patients store split tablets in bottles that previously contained the same medication, different medication or some other substance, or in the same bottle as whole tablets or in a dosage administration aid. Issues of concern relate to labelling of storage containers and the time that split tablets are exposed to air and light before use with the possible detrimental effect on stability. For example the instability of soluble aspirin limits the usefulness of the unused half of a split tablet. If only half the tablet is taken the unused half should be immediately discarded.

Patient-related factors

Tablets can be split manually into two portions by either breaking with the fingers along a scored line, cutting with a knife or using a specially designed tablet cutter. Substantial dexterity in positioning and holding the tablet is needed. Uneven division of the tablet or a degree of wastage can occur as some tablets may crumble or break into more than two parts.

Commercially available tablet cutters should increase the accuracy of tablet splitting, but these devices require a degree of manual dexterity in loading the tablet.[3] Irregularly shaped tablets may be difficult to load and may not easily be split into equal halves. Dividing a tablet into quarters is even more difficult and is likely to incur a greater rate of tablet wastage and inaccuracy in final dosage.[4]

Liquid formulations may not be suitable alternatives for elderly patients as measuring volumes of liquid formulations also requires dexterity and good eyesight. These formulations also preclude the use of dosage administration aids such as dispenser packs. Splitting tablets may be the only option when a reduced dose is needed.

Old age or diseases such as arthritis and Parkinson's disease can cause impaired manual dexterity or decreased grip strength that renders the process of splitting tablets extremely difficult.[5] Even if a tablet cutter is used it may not improve accuracy if the patient is functionally impaired. Cognitive impairment may make remembering instructions to split a tablet for a particular dose difficult, especially if dosage regimens are complex, such as tapering or increasing doses, or if more than one tablet is to be split.

Another issue of concern is whether difficulty splitting tablets may adversely affect patient compliance with drug regimens, as patients may skip or double doses rather than split tablets and retain unused halves. Complex regimens involving split tablets may be expected to decrease patient compliance. Studies have shown that patient compliance is not decreased by use of split tablet regimens[6,7], although the results should be interpreted with caution because of selection bias.

Cost considerations

While splitting tablets may appear cost-effective, there may be adverse consequences relating to the treatment of the patient's condition. Any savings from splitting tablets may be offset by drug wastage and potential negative effects on the quality use of medicines.

Conclusion

The decision to split tablets should be made after due consideration. The following recommendations may be used as a guide:

- Check the product information before recommending tablets be split
- In general only scored tablets should be split
- Patients should be assessed for their ability to understand and comply with regimens involving split tablets
- A tablet cutter can be used to improve accuracy, but patients must be instructed in its proper use
- Patients should be advised about appropriate storage of split tablets.

REFERENCES

1. McDevitt JT, Gurst AH, Chen Y. Accuracy of tablet splitting. Pharmacotherapy 1998;18:193-7.
2. Mandal TK. Effect of tablet integrity on the dissolution rate of sustained-release preparations. J Clin Pharm Ther 1996;21:155-7.
3. Carr-Lopez SM, Mallett MS, Morse T. The tablet splitter: barrier to compliance or cost-saving instrument? Am J Health Syst Pharm 1995;52:2707-8.
4. Horn LW, Kuhn RJ, Kanga JF. Evaluation of the reproducibility of tablet splitting to provide accurate doses for the pediatric population. J Pediatr Pharm Pract 1999;4:38-42.

5. Atkin PA, Finnegan TP, Ogle SJ, Shenfield GM. Functional ability of patients to manage medication packaging: a survey of geriatric inpatients. Age Ageing 1994;23:113-6.
6. Fawell NG, Cookson TL, Scranton SS. Relationship between tablet splitting and compliance, drug acquisition cost, and patient acceptance. Am J Health Syst Pharm 1999;56:2542-5.
7. Rindone JP. Evaluation of tablet-splitting in patients taking lisinopril for hypertension. J Clin Outcomes Manage 2000;7:22-4.

Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 151)

1. Splitting tablets can accelerate the degradation of the active ingredient.
2. If a soluble aspirin tablet is split the half which is not used immediately should be discarded.

Cisapride: more restrictions

Concerns about cardiac arrhythmias led to restrictions being placed on the prescription of cisapride.[1] There are few gastrointestinal conditions which require treatment with cisapride.[2] It should only be tried if patients with gastroparesis or severe gastro-oesophageal reflux have not responded to other drugs.

The manufacturer has now decided to withdraw the highest strength of cisapride tablets (20 mg). It has also revised the product information.

All patients now require measurements of renal function and ECGs before and during treatment. They should be followed up at least every three months. As interactions may prolong the QT_c interval, patients taking cisapride should be regularly asked if they are taking any other medicines.

REFERENCES

1. MacDonell D. Cisapride: new restrictions. Aust Prescr 2000;23:93.
2. Hebbard G, Gailer J, Young G. Alternatives to cisapride. Aust Prescr 2001;24:110-2.

Book review

Therapeutic Guidelines: Analgesic. Version 4. Melbourne: Therapeutic Guidelines Limited; 2002. 358 pages.
Price: $33, students $25.30, plus postage.*

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Analgesic guidelines can be used in two ways – as a detailed and useful resource about the physiology and pharmacology of pain and its management, and as an occasional resource for looking up specific disease states or painful conditions.

The list of contributors to Therapeutic Guidelines: Analgesic is impressive, and the writing style is concise and easy to read. It brings together the current understanding of the physiology of pain including pathways, neurotransmitters and pharmacology – what works where and how. There is also discussion of the psychology of pain.

Analgesics, adjuvants, physical therapies and psychological issues are all covered in this comprehensive review of all types of pain syndromes, to give a thorough overview of each topic.

This is demonstrated by considering the handling of the topic of headache, a common presenting problem for general practice. It starts with the presentation of warning signs for serious causes of headache, and has a table to help distinguish the benign causes of headache and their features.

Then discussed in detail with pathophysiology and management, are tension headache, migraine, cervical headache, occipital neuralgia, opioid addiction, drug induced headache, post-traumatic headache, cluster headache, chronic paroxysmal hemicrania, ice-pick headache, cough, exertional and sexual headache, and post-lumbar puncture headache. Facial pain and eye pain are handled separately in their own chapters.

In each case, discussion of the cause, and non-pharmacological and pharmacological management is detailed. There are also clear diagrams of neck exercises to show patients.

Other features include tables of drug interactions with all the significant classes of analgesics, pregnancy and breastfeeding classifications, tables of disease modifying antirheumatic drugs, local anaesthetic doses and characteristics, and the Glasgow Coma Scale. The management of cancer pain and palliative care issues are also included.

The index is accurate and effective, and combined with the straightforward chapter headings enables easy navigation.

This is a comprehensive resource that would suit a variety of levels from medical student to consultant. It can be read from cover to cover and used as a quick resource during a consultation. There are few texts that cover the range of analgesic topics in this depth. It is a valuable addition to the Therapeutic Guidelines series.

* For more information contact Therapeutic Guidelines Limited – 1800 061 260 or sales@tg.com.au