Solid Medication Dosage Form Modification at the Bedside and in the Pharmacy of Queensland Hospitals

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ABSTRACT

Background: Solid medication dosage forms are regularly modified to aid medication delivery to patients that are unable to swallow them.

Aim: To identify medications that are commonly modified in Queensland hospitals at the bedside and in the pharmacy and to identify how these modifications are made.

Method: A self-report survey was sent to 97 hospitals of varying sizes in metropolitan and rural areas across Queensland.

Results: Most ($n = 31$; 79%) of the responding hospitals reported that medications were modified at the bedside. 73 different medications were modified at the bedside. Most of the tablets or capsules had standard-release characteristics. 8 hospitals crushed modified-release dosage forms and 11 hospitals crushed medications with a narrow therapeutic index. At the bedside, 88% of medications were modified for adult use, mostly by crushing multiple tablets together (84% of hospitals) using a pestle and mortar (87%) and mixing into jam (72%) or water (64%). Only 7 hospitals reported modifications in the pharmacy (many small hospitals do not employ a pharmacist). 17 medications modified in the pharmacy were all modified for children because of the lack of commercial preparations.

Conclusion: Commercial medication dosage forms are altered in Queensland hospitals, including medications for which serious adverse effects may arise from the delivery of toxic or subtherapeutic doses. Pharmacists can contribute to the education of nurses to raise awareness of problems resulting from altering medication dosage forms. Education of doctors is also needed to raise awareness of prescribing alternative dosage forms that may either be commercially available or prepared by the pharmacy as an extemporaneous preparation.

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INTRODUCTION

Tablets and capsules are the solid dosage forms of choice for their ability to cheaply and accurately deliver a defined content of active pharmaceutical ingredient. Liquid dosage forms are usually more expensive per unit dose, may have physicochemical stability issues in the medium to long-term and it can be less easy to be sure of consistent measurement of accurate doses. However, for a considerable number of patients (particularly paediatric and geriatric) solid dosage forms are inappropriate, e.g. patients who are unable to swallow or dislike swallowing solid dosage forms, patients with nasogastric or gastrostomy feeding tubes, and patients who require non-standard doses.¹⁻⁴

In hospital practice, in response to the unavailability of commercial liquid dosage forms the pharmacy prepares extemporaneous oral liquid formulations. Extemporaneous preparations should ideally be made from raw ingredients, however, since pure crystalline powders are often not easily accessible to hospital pharmacies, a commercial solid dosage form is usually modified, i.e. tablets are crushed or capsules opened.^{5,6} Therefore, pharmacists must not only consider the active drug but also the inactive excipients contained in the solid dosage form when preparing the liquid formulation. For example, warfarin suspension prepared from crushed tablets is different from warfarin solution prepared from warfarin sodium powder.⁷ Isoniazid mixture must be prepared using isoniazid powder and not crushed tablets due to incompatibility caused by the tablet excipients.⁸

The problem of delivering a medication dose to a patient is felt directly by nurses, who commonly find themselves expected to deliver a solid dosage form to a patient who is unable to swallow it. It has been established that dosage form modifications occur in nursing homes and hospital wards, particularly for older mentally ill inpatients.⁹⁻¹³ The aim of this study was to identify medications that are commonly modified in Queensland hospitals at the bedside and in the pharmacy and to identify how these modifications are made.

METHOD

A self-report survey was distributed in July 2005 to all ($n = 97$) health facilities in Queensland, Australia, that are classified as hospitals by the Queensland Department of Health, i.e. have some inpatient beds. The survey contained open-ended questions formatted as a table to enable identification of the medications commonly modified at the bedside and in the pharmacy for each hospital. The survey asked for the reason and the methods used to modify the medication, the formulation or mixers used, the patient's age and the estimated frequency of modification. Respondents were also encouraged to comment or express their concerns.

A pilot study was undertaken using hospital pharmacists to ensure that the survey questions were appropriate. Each hospital was telephoned and a representative (e.g. pharmacist, director of nursing) was identified who would ensure completion of the survey. The surveys were then sent as a single mailing to that specific person. Surveys that were not returned were followed up twice by telephone to encourage survey completion.

As an indication of hospital size, the admission and non-admission activity data for the financial year July 2005 to June 2006 were collected from the Queensland Health web site.¹⁴ The Pharmacy Access/Remoteness Index of Australia (PhARIA) classification for 2006 to

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2007 for the area in which each hospital was located was collected.¹⁵ The PhARIA classification incorporates measurements of remoteness with a professional isolation component represented by the road distance to the five closest pharmacies. The index is divided into a six category classification system (1 = highly accessible, 2-3 = accessible, 4 = moderately accessible, 5 = remote and 6 = very remote).

Figure 1. Pharmacy Access/Remoteness Index of Australia (PhARIA) of the Queensland hospitals that responded to the survey categorised by the a) number of hospitals responding to the survey and those that have a pharmacist; b) number of hospitals that modify medication dose forms at the bedside or in the pharmacy; and c) percentage of hospitals that modify medications with sustained-release properties or a narrow therapeutic index.

RESULTS

The 39 (40%) hospitals that responded to the survey were spread across metropolitan and rural Queensland, with representation from all six PhARIAs (Figure 1a) and generally representative in terms of hospital size and remoteness. As might be expected, the responding hospitals located in metropolitan centres (PhARIA 1) were larger, with greater annual admission and non-admission activity than hospitals located in rural areas (Figure 2). Only nine of the responding hospitals had a pharmacy staffed by a pharmacist at the time of the survey (Figure 1a).

Figure 2. Categorisation of the responding hospitals in terms of the Pharmacy Access/Remoteness Index of Australia (PhARIA) for the a) mean ± SE number of beds; b) mean ± SE number of admissions; and c) mean ± SE non-admission activity during the financial year 2005/06.

Table 1. Medications commonly modified at the bedside or in the pharmacy of Queensland hospitals

Active pharmaceutical ingredient	ATC classification	No. of hospitals	Patients	Starting material	Mixer
<i>Modified at the Bedside</i>					
Amlodipine	C8	4	Adult/Child	CT	Jam, food, water
Aspirin	B1	7	Adult	CT	Jam, custard, food, water
Atenolol	C7	4	Adult	CT	Jam, custard, yoghurt, water
Digoxin	C1	5	Adult/Child	CT	Jam, thickened fluid, custard, food, juice, water
Dipyridamole + aspirin	B1	4	Adult	OC	Jam, thickened fluid, food, juice, water
Docusate + senna	A6	5	Adult	CT	Jam, honey, custard, food, water
Fruzemide	C3	6	Adult	CT/ST	Jam, food, water
Multivitamins	A11	5	Adult	CT	Jam, honey, thickened fluid, food, juice, water
Omeprazole	A2	7	Adult/Child	OC/CT	Jam, honey, custard, food, water
Paracetamol	N2	18	Adult/Child	CT/ST	Jam, honey, thickened fluid, custard, food, juice, water
Perindopril	C9	8	Adult/Child	CT/ST	Jam, honey, thickened fluid, custard, food, juice, water
Risperidone	N5	4	Adult	CT	Jam, custard, yoghurt
Sertraline	N6	4	Adult	CT	Jam, honey, food
<i>Modified in the Pharmacy</i>					
Amiodarone	C1	2	Child	CT	Extemporaneous preparation
Metoprolol	C7	2	Child	CT	Extemporaneous preparation
Omeprazole	A2	2	Child	DT	Extemporaneous preparation
Propranolol	C7	2	Child	CT	Extemporaneous preparation
Sildenafil	C2	2	Child	CT	Extemporaneous preparation
Sotalol	C7	2	Child	CT	Extemporaneous preparation
Spironolactone	C3	3	Child	CT	Extemporaneous preparation
Tacrolimus	L4	2	Child/Adult	OC	Extemporaneous preparation

ATC = Anatomical Therapeutic Chemical. CT = crushed tablet. DT = dispersed tablet. OC = opened capsule. ST = split tablet.

Modifications at the Bedside

Most (n = 31; 79%) of the hospitals reported that medications were modified at the bedside (Figure 1b). Of these, six hospitals reported that many medications were modified without stating any specific examples. Only a few hospitals (n = 8; 21%) located within PhARIA 3 to 6, reported that they never modified medication dosage forms.

Seventy-three different medications were identified by the 25 hospitals as being modified at the bedside. Most of the medications were for treating complaints of the nervous system, cardiovascular system or alimentary tract and metabolism (Table 1). Paracetamol tablets were most frequently modified, mostly crushed or occasionally split into pieces and added to a variety of mixers in 70% of the hospitals. Omeprazole (Probitor) was the most commonly opened capsule; four out of six hospitals sprinkled the enteric-coated pellets into a mixer and two hospitals crushed the enteric-coated pellets before adding water for nasogastric or gastrostomy tube feeding. One hospital preferred to crush omeprazole (Losec) tablets before adding to the mixer and one hospital crushed pantoprazole (SOMAC) tablets.

Most of the modified tablets or capsules did not have controlled-release or sustained-release properties. For example, the brands of metoprolol used by the hospitals did not have controlled-release characteristics. Furthermore, five of the six hospitals that did not give any specific examples of medications that they modified

did note that controlled-release or sustained-release dosage forms were not among those modified. However, there were a small number of controlled-release or sustained-release dosage forms that were crushed at the bedside in this survey (Figure 1c). Four hospitals opened dipyridamole+aspirin capsules (Asasantin SR), with two of these hospitals crushing the contents, three hospitals crushed iron+folic acid controlled-release tablets (FGF), two hospitals opened venlafaxine (Efexor) capsules, and there was one report for each for morphine (MS Contin), nifedipine (Adalat Oros) and verapamil (Veracaps).

Most (88%) of the 73 medications were modified at the bedside for adults; seven medications were modified for adults and children and nine medications were modified for children. Apart from paracetamol, all of the modifications for children were made by specialist paediatric hospitals. The main reason for modification at the bedside given for 60 (82%) of the medications was the inability of the patient to swallow the solid dosage form. Other reasons for modification included the correct dose was not commercially available (10 medicines; 14%) or there was a need for a liquid dosage form for tube feeding (38 medicines; 52%); the latter was the sole reason for modification of eight (11%) of the medications.

Hospitals mostly used a mortar and pestle to crush tablets (n = 27). Some hospitals crushed tablets between spoons (n = 5) or used a commercial tablet crushing device (n = 3). For example, paracetamol tablets were split into pieces by three hospitals, crushed between spoons by

two hospitals, but most of the hospitals (n = 13) used a pestle and mortar. Capsules were invariably opened and the contents sprinkled into the mixer. Many hospitals (n = 21) crushed and mixed two or more medications together, providing the patient with a single mixer containing multiple medications. A variety of mixers were used by the hospitals (Table 1) and the most common mixers were jam (n = 18), water (n = 16) and sprinkling or mixing into the patient's food (n = 12). Less commonly used mixers were honey (n = 5), thickened fluid (n = 3), juice (n = 3), custard (n = 2) and yoghurt (n = 1).

Modifications in the Pharmacy

Only seven of the 39 responding hospitals reported modifying solid dosage forms in the pharmacy. This is largely due to the lack of a pharmacist on-site; only two of the hospitals in PhARIA 2 to 6 were large enough to have a pharmacist, while seven of the nine PhARIA 1 hospitals had a pharmacist (Figure 1a).

Five of the seven PhARIA 1 hospitals modified dosage forms in the pharmacy. All of these hospitals were large (> 150 beds), had a pharmacist and used the *Australian Pharmaceutical Formulary and Handbook* or a hospital formulary. The other two hospitals that modified dosage forms in the pharmacy were from PhARIA 2 and 6 and do not have a pharmacist. Both of these hospitals regularly made a paediatric preparation (omeprazole or propranolol) because the correct dose was unavailable. Nurses at these hospitals followed the formulas provided to them by larger hospitals.

Of the 17 medications modified in the pharmacy, twelve medications were different to those modified at the bedside and eight medications were modified by two or three of the seven hospitals (Table 1). Most of the medications were for treatment of the cardiovascular system. All except three of the 17 medications were modified by crushing tablets – phenoxybenzamine (Dibenyline) and tacrolimus capsules were opened, and

one hospital modified desmopressin nasal spray (Minirin). The only controlled-release formulation to be modified was omeprazole; tablets were crushed prior to compounding.

All of the medications were modified so that they could be taken by children; only one medication (tacrolimus) was also modified for adults by two hospitals. All of the 17 medications were modified because of the lack of an appropriate dose; for three medications the need for a liquid preparation for tube feeding was an alternative reason. Both inpatients and outpatients were recipients of modified medications.

DISCUSSION

This survey covered a cross-section of Queensland, with hospitals responding from very remote locations through to highly accessible metropolitan areas. Modifications are made to commercial medication dosage forms on the hospital wards throughout Queensland, with 79% of the hospitals reporting that nursing staff crush tablets and open capsules to help patients take their medications. As a self-report survey, rather than an audit of nursing and pharmacy practice in each hospital, we were reliant on knowledge of hospital practices and honesty by the staff members completing the survey. Therefore, the results are indicative of what was happening within the responding hospitals at the time of the survey. It is possible that this is an underestimation of the actual extent of modification and the range of medications being modified in Queensland.

Medications that are controlled-release, sustained-release or modified-release should not be altered because of the toxicity that can result from faster absorption when the coating is disrupted. A number of hospitals specifically mentioned that these dosage forms were not among those that they modified. However, the message is not reaching all nursing staff, as in eight hospitals some of these medications were modified inappropriately.

Table 2. Potential risks associated with medications modified by Queensland hospitals

Potential risks	Dosage form modifications	Medications
Increased toxicity or adverse effects	Crushing an extended/modified/sustained-release formulation.	Dipyridamole+aspirin (Asasantin SR), iron+folic acid (FGF), morphine (MS Contin), nifedipine (Adalat Oros), venlafaxine (Efexor), verapamil (Veracaps)
	Crushing a coating designed to protect the upper gastrointestinal tract from the active pharmaceutical ingredient.	Iron+folic acid (FGF), metronidazole, valproate
	Crushing a coating designed to disguise a poor tasting active pharmaceutical ingredient.	Ibuprofen, topiramate
Decreased efficacy	Crushing an enteric coating designed to protect an acid-labile active pharmaceutical ingredient.	Omeprazole, pantoprazole
	Crushing a coating designed to protect a light or air sensitive active pharmaceutical ingredient.	Nifedipine (Adalat Oros)
	Crushing a coating designed to release the active pharmaceutical ingredient at a defined site in the gastrointestinal tract.	Omeprazole, pantoprazole
	Incomplete dose delivery for an active pharmaceutical ingredient with a narrow therapeutic index.	Carbamazepine, digoxin, thyroxine, valproate, warfarin
	Crushing and mixing with food when 'take on an empty stomach' is advised.	Fruzemide, pravastatin, thyroxine
Hazards to health workers	Crushing a dose form containing a cytotoxic or teratogenic active pharmaceutical ingredient.	Azathioprine, tamoxifen
Breach of legal and professional requirements	Modifying the medication is deemed to be unlicensed.	Most of the medications

These occurrences were not associated with small hospitals or remote regions (Figure 1), and the three hospitals in PhARIA 1 reporting this conduct all had a pharmacist.

Tablet coatings possess other functions and modification has the potential to cause undesirable adverse effects or decreased efficacy (Table 2). Tablet coatings may protect the stomach lining from an irritant drug or make a poor tasting drug more palatable, and removing the barrier will reduce compliance or result in unwanted adverse effects. For example, crushing prednisolone tablets, which have a bitter taste, results in poor compliance in paediatric patients and formulation of a prednisolone oral solution is a better option.¹⁶ Tablet coatings may protect the drug from the environment and removing this protection may result in drug inactivation or reduced absorption. Proton pump inhibitors are a classic example because the drug molecules are acid-labile and must be protected from exposure to an acid environment until they reach the site of action.¹⁷ These medications were generally handled appropriately, with the enteric-coated granules left intact; nurses had more of a problem dealing with these medications when administration via feeding tube was required.

For most of the medications in this study, the dosage form had no special property and would be considered standard disintegrating tablets. However, an issue that is often overlooked is the reduction of efficacy due to incomplete and inconsistent dosage administration resulting from losses during the crushing and administration process (Table 2). While for many medications a slight reduction in dose may not be critical, for drugs with a narrow therapeutic index any change in dosage can be vital. For example, losses of oral thyroxine occur when tablets are crushed and given via a feeding tube resulting in a hypothyroid state; the reduced dose delivery is not due to the adsorption of thyroxine onto the feeding tubes and has been suggested to be due to losses during crushing and transfer into the tube.¹⁸

In this study, there was no association between the location of hospitals in terms of PhARIA and likelihood to crush a medication with a narrow therapeutic index (Figure 1). It is notable that none of the eleven hospitals that reported modifying medications with a narrow therapeutic index have a pharmacist. Although the product information for most of the medications in this study does not explicitly state not to crush, they also do not explicitly say that it can be done, so any modification of the original dosage form makes it off-licence and the manufacturer assumes no liability for any ensuing harm that may befall the patient.^{19,20}

Modifications at the bedside involved the use of a variety of mixers – jam and water were popular choices. The effect of food on drug absorption may not be a consideration in most cases, but instructions for some medications specify ‘take on an empty stomach’ and so are more likely to be involved in a drug–food interaction (Table 2). Problems are most likely to occur when the hospital practice of crushing and mixing with food or semisolid mixers is discontinued or changed when the patient leaves hospital. As such, continuity of care, safety and quality can become major issues.

For some of the medications that were crushed at the bedside, an alternative dosage form exists that is more easily swallowed, e.g. suspensions or dispersible tablets. Amoxycillin, carbamazepine, frusemide, haloperidol, metronidazole and valproate tablets were crushed at the bedside in some hospitals despite the existence of a liquid formulation. If no liquid formulation exists, an alternative route of administration (e.g. prochlorperazine suppositories instead of tablets) or a therapeutic alternative that is available as a smaller tablet or as an alternative dosage form, may be appropriate.

Patients should not be denied useful medicines simply because there are no suitable commercial dosage forms. Formulation of extemporaneous preparations by a pharmacy may be an alternative, as multi-dose formulations remove the need for daily tablet-crushing at the bedside and reduce the possibility for dosage error or cross-contamination. Liquid dosage forms can be provided that are easier to swallow and more palatable than crushed tablets, for example, the contents of oseltamivir capsules can be bitter and better provided as flavoured syrup.²¹ Furthermore, medications such as cytotoxics may be harmful to health workers involved in crushing tablets, so modification in the pharmacy would be more appropriate than on the ward.^{22,23} Of the medications that were crushed at the bedside in this study, 13 could have been extemporaneously prepared based on recently reviewed formulations for which stability has been established.³ Additionally, the *Australian Pharmaceutical Formulary and Handbook* outlines a six-step process to assist pharmacists in the modification of oral formulations, including information on medications that should not be altered.²⁴

Queensland hospitals that have a pharmacist on-site are regularly involved in extemporaneous compounding, with commercial dosage forms being the starting material in 70% of formulations.⁵ Preparation of extemporaneous formulations in this study was limited by the lack of a pharmacist on-site for many of the responding hospitals, a situation that is common in non-urban regions of Australia. Community pharmacies could be employed in these situations to prepare appropriate formulations. It is apparent that the pharmacies in the hospitals that responded to this survey were being asked to prepare formulations for dose adjustment for their paediatric patients, while on the wards nurses were crushing medications for adult patients with swallowing difficulties. There is a lack of knowledge on the part of prescribers regarding the potential for using the services of pharmacists to make extemporaneous preparations.²⁵

In conclusion, while doctors continue to prescribe solid dosage forms, nursing staff will continue to find themselves in the unenviable situation of delivering a medication that a patient cannot swallow. Pharmacists can contribute to the education of nurses to raise awareness of problems resulting from altering medication dosage forms. Education of doctors is also needed to raise awareness of prescribing alternative dosage forms that may either be commercially available or prepared by the pharmacy as an extemporaneous preparation.

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