Conformity of commercial oral single solid unit dose packages in hospital pharmacy practice

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Abstract

Background. There are limited published data on the labelling of single unit dose packages in hospitals.

Setting and participants. The study was conducted in three large hospitals (two adult and one paediatric) in the metropolitan Montreal area, Quebec, Canada.

Objective. The objective is to evaluate the labelling of commercial oral single solid unit dose packages available in Canadian urban hospital pharmacy practice.

Method. The study endpoint was the labelling conformity of each unit dose package for each criterion and overall for each manufacturer. Complete labelling of unit dose packages should include the following information: (1) brand name, (2) international non-proprietary name or generic name, (3) dosage, (4) pharmaceutical form, (5) manufacturer’s name, (6) expiry date, (7) batch number and (8) drug identification number. We also evaluated the ease with which a single unit dose package is detached from a multiple unit dose package for quick, easy and safe use by pharmacy staff. Conformity levels were compared between brand-name and generic packages.

Results. A total of 124 different unit dose packages were evaluated. The level of conformity of each criterion varied between 19 and 50%. Only 43% of unit dose packages provided an easy-to-detach system for single doses. Among the 14 manufacturers with three or more unit dose packages evaluated, eight (57%) had a conformity level less than 50%.

Conclusion. This study describes the conformity of commercial oral single solid unit dose packages in hospital pharmacy practice in Quebec. A large proportion of unit dose packages do not conform to a set of nine criteria set out in the guidelines of the American Society of Health-System Pharmacists and the Canadian Society of Hospital Pharmacists.

Keywords: blister packaging, bulk, drug packaging and labeling, unit dose package

Introduction

In Canada and the USA, most hospital pharmacy departments provide a daily unit dose drug distribution system for inpatients [1, 2]. This distribution system has been in wide use since the 1970s, and most publications related to the implementation and evaluation of such systems were published in the 1970s and 1980s [3–6]. A failure mode and effects analysis to improve drug distribution suggests that the percentage of opportunities during which any error occurred was significantly lower under the unit dose drug distribution system [7].

The Institute of Medicine recommends the implementation of a unit dose drug distribution system as a medication safety strategy to reduce errors in health care [8]. The Medicines and Healthcare Products Regulatory Agency has issued guidelines for drug manufacturers. The International Pharmaceutical Federation, the Institute for Safe Medication Practices (ISMP), the American Society of Health-System Pharmacists (ASHP) and the Canadian Society of Hospital Pharmacists (CSHP) have published their statements and guidelines on unit dose drug distribution [9–12]. According to an ASHP statement on unit dose drug distribution, ‘the unit dose system may differ in form, depending on the specific needs of the organization. However, the following distinctive elements are basic to all unit dose systems: medications are contained in single unit packages; they are dispensed in as ready-to-administer form as possible; and for
most medications, not more than a 24-hour supply of doses is delivered to or available at the patient-care area at any time’ [9]. Joint Commission on Accreditation of Healthcare Organizations standards require ‘medications to be dispensed in the most ready-to-administer form possible to minimize opportunities for error’ [13].

According to the ASHP Technical Assistance Bulletin on Single Unit and Unit Dose Packages of Drugs, drugs packages must fulfill four basic functions: identify their contents completely and precisely, protect their contents from deleterious environmental effects (e.g. photodecomposition), protect their contents from deterioration due to handling (e.g. breakage and contamination) and permit their contents to be used quickly, easily and safely [10]. According to CSHP guidelines for drug packaging and labeling for manufacturers, a unit dose is a package that contains a particular dose of drug ordered for a patient, that is fully identified and that is ready for administration directly from the package [12]. According to the guidelines, the mandatory label components of each unit dose package include the common or brand name for multiple active ingredient products, strength, lot number, name of the manufacturer and expiry date. Furthermore, the unit dose package must be able to be easily opened and the medication easily removed from the package to be administered directly to the patient. Push-through packages should not be used because the label is destroyed when the tablet or capsule is removed. Interestingly, Cohen says that the United States Pharmacopeia and Food and Drug Administration should standardize the terminology used on labels. Both ‘single-use and single dose have been used on containers labels to mean the same thing’. He also says that ‘regardless of a product’s prescription or non-prescription status, the name and exact strength should be present on each pocket [referred to as a single unit dose package in our text] of the blister strip. Whether or not the manufacturer intends this, many nonprescription drugs are used in institutions as part of a unit dose dispensing system. [...] The blisters can be cut and separated from one another, or the drug name may be torn, making identification impossible and contributing to subsequent errors if the product is relabeled extemporaneously’ [14].

Hospital pharmacists can buy drugs in bulk format or unit dose packages. Bulk format contains unpacked drugs that can be repacked by an automated medication dispensing system (Pacmed™, Automed™, etc.). Multiple unit dose packages are split (detached or cut) in single unit dose packages. In an unknown proportion of cases, the labeling of the detached single unit dose package is not complete for safe medication use in hospitals. Any missing information on a single unit dose package can lead to medication errors (wrong medication, wrong patient, expired medication, improper handling of a returned medication) [15–19].

There are limited published data on the labeling of single unit dose packages in hospitals. The objective of this study is to evaluate the labeling of commercial oral single solid unit dose packages available in urban hospital pharmacy practice in Canada.

Methods

This is an observational study based on the visual inspection of commercial oral single solid unit dose packages (hereafter unit dose package) available in three large hospitals in the metropolitan Montreal area, Quebec, Canada. The three hospitals included are representative of major acute care settings in Quebec (e.g. two large adult teaching hospitals with 637 and 571 beds each and one large mother-child university hospital center with 500 beds). These hospitals purchase drugs primarily through Approvisionnement Montréal, the second largest drug-purchasing group in Canada. We identified all unit dose packages available in the 2006–2009 hospital purchasing agreement catalog. In July 2005, a pharmacy research assistant visited three pharmacy departments in order to locate, visually identify and evaluate all unit dose packages in stock. Each hospital included in this study uses an automated packaging system and has a daily unit dose drug distribution system. Whenever listed in the agreement catalog, the three hospitals purchase drugs in bulk to take advantage of their automated medication system. Usually, drugs purchased in unit dose packages are the only format available. Based on our literature search, a group of three pharmacists selected nine conformity criteria for unit dose packages used in a daily hospital unit dose drug distribution system. Complete labeling of unit dose packages should include the following information: (1) brand name, (2) international nonproprietary name or generic name, (3) dosage, (4) pharmaceutical form, (5) manufacturer’s name, (6) expiry date, (7) batch number and (8) drug identification number. We also evaluated the (9) ease with which a single unit dose package is detached from a multiple unit dose package to allow quick, easy and safe use by pharmacy staff. Based on visual inspection, the conformity of each unit dose package was assessed at each site visited and a digital photograph of both sides of each unit dose package was taken. The study endpoint was the labeling conformity of each unit dose package for each criterion and overall for each manufacturer. Conformity levels were compared between brand and generic packages. The overall score of conformity per manufacturer is the average of the score of conformity of each criterion with a maximum of 100% (0–100% per criterion for a total of nine criteria) for manufacturers with three or more drugs evaluated. Data were entered in a spreadsheet (Microsoft Excel®, Seattle, USA 2003). Statistical analysis was performed with SPSS 15.0. (SPSS Inc., 2007). A $P < 0.05$ was considered significant.

Results

A total of 374 unit dose packages were identified from Approvisionnement-Montréal’s 2006–2009 catalog. A total of 124 (33%) different unit dose packages were physically located in the three hospitals visited for visual inspection. Criterion’s conformity level varied from 19 to 50% for all manufacturers, 13 to 42% for brand manufacturers and 41
to 85% for generic manufacturers (Table 1). Only 43% of unit dose packages provided an easy-to-detach system for single doses. Examples of conforming and nonconforming unit dose packages are given in Table 2.

The lowest average score of conformity for all criteria for a manufacturer (with three or more drugs evaluated) was 0% (Léopharma and Servier) and the highest was 90% (Apotex). Among the 14 manufacturers with three or more unit dose packages evaluated, eight (57%) had a conformity level less than 50%. For all criteria, except the presence of a brand name, the 27 unit dose packages from generic manufacturers had a higher level of conformity than the 97 produced by brand manufacturers ($P = 0.002$). However, some brand manufacturers had better scores than others (e.g., Merck Frosst, Bayer). Apotex had the highest level of conformity and the highest number of solid drug packages evaluated.

Table 1 Number and proportion of commercial oral single solid unit dose packages that conform to nine criteria ($n = 124$) and according to the type of manufacturer

<table>
<thead>
<tr>
<th>Conformity criteria for unit dose package</th>
<th>Number (proportion) of unit dose packages that conform to criteria</th>
<th>All manufacturers ($n = 124$)</th>
<th>Brand name ($n = 97$)</th>
<th>Generic ($n = 27$)</th>
<th>Comparison between brand and generic manufacturers, $P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of a brand name</td>
<td></td>
<td>56(45)</td>
<td>40(42)</td>
<td>15(56)</td>
<td>&lt;0.28</td>
</tr>
<tr>
<td>Presence of international non proprietary name</td>
<td></td>
<td>53(43)</td>
<td>34(35)</td>
<td>22(82)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence of dosage</td>
<td></td>
<td>62(50)</td>
<td>40(41)</td>
<td>22(82)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence of pharmaceutical form</td>
<td></td>
<td>24(19)</td>
<td>13(13)</td>
<td>11(41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence of manufacturer's name</td>
<td></td>
<td>52(42)</td>
<td>31(32)</td>
<td>21(78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence of expiry date</td>
<td></td>
<td>53(43)</td>
<td>30(31)</td>
<td>23(85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence of batch/lot number</td>
<td></td>
<td>53(43)</td>
<td>30(31)</td>
<td>23(85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence of drug identification number</td>
<td></td>
<td>32(26)</td>
<td>18(18)</td>
<td>15(56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ease with which single unit is detached from multiple dose package</td>
<td></td>
<td>53(43)</td>
<td>33(34)</td>
<td>19(70)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2 Examples of criteria conformity of commercial oral single solid unit dose packages

<table>
<thead>
<tr>
<th>Conformity criteria</th>
<th>Cyclosporine 25 mg(Neoral®) – Novartis Pharma Canada, Inc.</th>
<th>Fenofibrate 160 mg(Lipidil Supra®) – Fournier Pharma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of a brand name</td>
<td>Conform</td>
<td>Non conform</td>
</tr>
<tr>
<td>Presence of international non proprietary name</td>
<td>Conform</td>
<td>Non conform</td>
</tr>
<tr>
<td>Presence of dosage</td>
<td>Conform</td>
<td>Non conform</td>
</tr>
<tr>
<td>Presence of pharmaceutical form</td>
<td>Non conform</td>
<td>Non conform</td>
</tr>
<tr>
<td>Presence of manufacturer's name</td>
<td>Conform</td>
<td>Non conform</td>
</tr>
<tr>
<td>Presence of expiry date</td>
<td>Conform</td>
<td>Non conform</td>
</tr>
<tr>
<td>Presence of batch/lot number</td>
<td>Conform</td>
<td>Non conform</td>
</tr>
<tr>
<td>Presence of drug identification number</td>
<td>Non conform</td>
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</tr>
<tr>
<td>Ease with which single unit is detached from multiple dose package</td>
<td>Conform</td>
<td>Non conform</td>
</tr>
</tbody>
</table>
Discussion

This study describes the conformity of commercial oral single solid unit dose packages in hospital pharmacy practice in Quebec. A large proportion of unit doses packages do not conform to a set of nine criteria set out in the guidelines of the ASHP and the CSHP. In the Canadian context, the low conformity of labeling of unit dose packages can be partly explained by the fact that the Canadian Food and Drug Act regulates outside and inside labeling of multiple dose packages, but not specifically single unit dose packages that can be detached and used in hospital settings.

Our study indicates that for all criteria, except for the presence of a brand name, unit dose packages from generic manufacturers had a higher level of conformity than those produced by the brand-name manufacturers. Based upon our hospital group purchasing activities, we postulate that the generic industry is more pharmacy-oriented when it comes to differentiating their products and fulfilling hospital needs.

In a survey of US state boards of pharmacy in 2003 pertaining to the status of multiple dose packages (also called blister packages), approximately two-thirds of respondents believed that multiple dose packaging would improve efficiency, reduce errors in dispensing, improve patient compliance and increase opportunities for patient counseling in community pharmacy practice [20]. Supporters of multiple unit dose packages have mentioned its potential positive effect on patient compliance. In a community setting, multiple unit dose packages can also contribute to reinforce the brand-name identity of a drug. Although the use of multiple unit dose packages can improve efficiency for retail pharmacy activities, hospital pharmacists have different needs and there are no published reports describing the difficulties inherent to the nonconformity of single unit dose packages in hospital settings.

In Europe, the majority of drugs are packaged in multiple unit dose packages for retail and hospital settings. The limited penetration of unit dose drug distribution systems in hospitals has not exerted any significant pressure on manufacturers to maintain a bulk format available for nominal daily drug distribution. Indeed, problems with multiple unit dose packages have not been reported in the European context. Interestingly, some companies have developed deblistering machines (e.g., www.pentapackna.com) to unpack multiple unit dose packages for automated medication systems. Alternatively, manual deblistering can be processed by pharmacy staff, although it is time consuming and requires cutters, and there is a risk of staff injury, as some packages can be edged. Aside from the inherent risk of injury, this process is unproductive and could lead to dispensing doses with incomplete relevant information or expired drugs if the unit dose package, when detached from the multiple unit dose package, does not conform.

There are few published data regarding the impact of the labeling of single unit dose packages in hospitals. Medication errors in hospitals have received considerable attention, as they entail significant mortality, morbidity and additional healthcare costs. In the Canadian Adverse Events Study [21], the overall incidence of adverse events was 7.5%. Of the 360 events identified, 85 were drug or fluid related. Medication errors can occur from prescribing (49–68%) or distributing and administering drugs (9–51%) [22]. The hospital pharmacist is best placed to oversee the quality of the entire drug distribution circuit, from prescribing, selecting and dispensing through to preparing and administering drugs [15]. Drug labeling is an important component of the drug distribution circuit to avoid medication errors in the pharmacy or at the bedside. Kenagy et al. state that the ISMP receives 1200–1500 reports of serious complications resulting from the use of drugs. Approximately 25% of these are related to name confusion and another 25% to labeling and packaging issues [23]. The authors point out that the ISMP estimates only 1–2% of events are reported. In their 2001 medication error report to the Food and Drug Administration, Thomas and Holquist calculate that 20% of medication errors are related to labeling and 6% to packaging and design [24]. In a review published by Berman, up to 25% of all medication errors are attributed to name confusion and 33% to packaging and/or labeling confusion [19]. In annual review about the labeling and packaging of drugs, La Revue Prescrire states that more than 90% of multiple unit dose packages (blister packs) are not appropriate for single unit doses [25].

The National Coordination Council for Medication Error Reporting and Prevention has made a series of recommendations for medication labeling and packaging that may help to reduce the incidence of medication errors. Among these recommendations, collaboration is called for among industry, regulators, standard-setters, healthcare professionals, healthcare organizations and patients to facilitate the design of packaging and labeling to help minimize errors. Another report indicated that confusing, inaccurate or incomplete drug labeling contributed to 21% of potential or actual medication errors reported through the US Pharmacopeia Practitioner’s Reporting Network over a one year period [18]. Very few cases of errors related to labeling and packaging have been published. For example, Guchelaar et al. reported a case in which the patient had been given a double dose of valaciclovir due to the ambiguous labeling of a commercial drug [15]. Pathak et al. reported confusion between amiodarone and acebutolol by confusing generic drug blisters that often have the same appearance to minimize costs [16].

This study does have its limitations. We evaluated a selection of all commercial oral single solid unit dose packages located in three large hospitals of a metropolitan area in Canada. A representative sample including all provinces would be more appropriate, although the same drugs are available across the country. The discrepancy observed between the number of unit dose packages listed in the hospital purchasing agreement catalog (n = 374 unit dose packages) and the number of packages included in this study (n = 124) can be explained by local hospital decisions not to purchase some of the drugs and having other formats or
molecules listed in their hospital formulary. Moreover, the results apply to the Canadian context and may differ in other jurisdictions, as labeling and marketing policies differ from country to country. This study did not evaluate the conformity of unit dose packages produced, repacked and labeled by pharmacy departments through their in-house systems.

This study describes the emergence of a nonconforming format that requires repackaging in hospital pharmacy practice and that could be avoided through better collaboration between pharmacy manufacturers and hospital pharmacists.

**Conclusion**

This study describes the conformity of commercial oral single solid unit dose packages in hospital pharmacy practice in Quebec. A large proportion of unit doses packages do not conform to a set of nine criteria set out in the guidelines of the ASHP and the CSHP.

**References**


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