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REVIEW

Stability of chronic medicines in dosage administration aids. How much have been done?

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KEYWORDS

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Abstract *Background:* The prevalence of chronic diseases is increasing in Asia, therefore compliance to the medications is of utmost importance to slow disease progression and improve outcomes. Dosage administration aids (DAAs) serve as important tool to improve the compliance of patients. However, there is a dearth of data on the stability of chronic medications in DAAs. Furthermore, data presented by our Western counterparts may not be applicable to us because of our extreme humidity and temperature. In this study, we aim to summarize the data available in the literature on the stability of chronic medications in DAA.

Methods: We performed a literature search using electronic databases and related keywords.

Results: In total, 24,336 articles were retrieved and 21 articles were found to be relevant to our topic. This commentary stratified drugs according to their treatment categories and key stability conclusions, DAA and conditions used and recommendations were presented.

Conclusion: Due to the lack of specific data, pharmacists have to exercise their professional judgment with the help from professional guidelines when using DAA in repackaging medication. Manufacturers and regulators can play a greater role in filling the gap needed to provide pharmacists with necessary information to fulfill their function.

Contents

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1. Introduction

Prevalence of chronic diseases is rising in Asia and compliance to medication is necessary to ensure slowing of disease progression as well as improving healthcare outcomes (Tan, 2011). In Asia, the number of people needing dosage administration aid (DAA) to assist in medication administration is increasing (Brown and Bussell, 2011). Reminder packaging, dosette, doset, multi-compartment compliance aids (MCAA) or compliance aid all refer to DAA. DAA is defined as a device that assists patients in managing their medicines by having patients, caregivers, or pharmacists, to arrange individual doses according to their prescribed dose regime throughout the day for certain duration of time. There were many studies that had shown favorable outcomes when patients used DAA to help them improve their adherence to medications (Rivers, 1992). Studies had shown that DAA helped to reduce medication error rates during medication administration in nursing homes, useful to simplify patients' medication regime and may overcome barriers to adherence such as difficulties in reading pharmacy labels and opening medication containers (Roughead et al., 2003; Cramer, 1998; Kippen et al., 2005; van Eijken et al., 2003). There were reports showing that DAA use helps to improve clinical outcomes like glycemic, blood pressure and lipids control (Simmons et al., 2000; Lee et al., 2006).

In Asia, especially Singapore, the weather is extremely humid and of high temperature all year round. An average relative humidity (RH) in Singapore can range from 80% to 100%, while temperature ranges from 25 to 30 °C (Pinto et al., 2011). World Health Organization's stability guidelines stated that certain Asian countries have long-term stability conditions of 30 °C and 75% RH (Bott and Oliveira, 2007). This differs greatly from the conditions of the Western countries and therefore, may need a different set of stability data so that pharmacists can determine if a particular drug will be suitable to be stored in a DAA. Repackaging of a medicine requires removal from its primary packaging, thus invalidates the stability guarantee by the manufacturer. Manufacturers also tend to discourage repackaging because there is little data to support this action (Church and Smith, 2006). As far as we know, there are very limited studies on the stability of drugs when repackaged into a unit dosing system and this is especially so in the context of Asia. With the increase in the prevalence of chronic diseases in Asia, data for repackaging of medicine into DAA will be essential so that the medicine manufactured will be of suitable physical, chemical and photo stabilities.

Therefore, the aim of this commentary is to provide readers a summary of the types of stability data available. Manufacturers and regulators, especially that of Asian countries, will be able to conduct more region specific stability studies to fill the gap needed to provide the pharmacists with essential data to support their operations. In turn, the patients' compliance can be improved, disease progression can be slowed and improved healthcare outcomes can be delivered.

2. Methods

An electronic database search was performed using Pubmed, Google Scholar, Web of Science, Scopus and ScienceDirect. Hand searches were also conducted using the references of related articles. Searches were current as of June 2013. The keywords utilized were (''dosage administration aid'' OR ''reminder packaging'' OR dosette OR doset OR repackaged OR ''compliance aid'') AND (stability OR duration OR characteristics OR degradation OR ''color changes''). There were no exclusion criteria due to the dearth of literature on the topic and all related articles were reviewed.

3. Results

3.1. Search results

A total of 24,336 articles were retrieved from our searches. Twenty-one articles were found to be relevant to our topic.

3.2. Cardiovascular medications

Studies were found for 4 cardiovascular drugs, namely metoprolol, atenolol, frusemide and aspirin. A summary can be found in Table 1.

Metoprolol is a beta-blocker used to treat several diseases of the cardiovascular system such as hypertension. From the study published by Yang et al., controlled and accelerated test conditions are 25 °C/60% RH and 40 °C/75% RH, respectively. The DAA of interest was the United States Pharmacopoeia (USP) Class A unit dose blister pack. Tablets were stored at accelerated and controlled conditions for 52 weeks and 12 weeks respectively. USP standards for chemical stability were met for all conditions and packaging. However, water uptake and tablet hardness increased for repackaged tablets stored in accelerated conditions (Yang et al., 2010).