ORIGINAL ARTICLE

The usefulness and scientific accuracy of private sector Arabic language patient drug information leaflets

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Abstract  Background: Inadequate access to useful scientifically accurate patient information is a major cause of the inappropriate use of drugs resulting in serious personal injury and related costs to the health care system. The definition of useful scientifically accurate patient information for prescription drugs was accepted by the US Secretary of the Department of Health and Human Services in 1996 as that derived from or consistent with the US FDA approved professional product label for a drug. Previous quality content studies found that English language patient drug information leaflets distributed by US pharmacies failed to meet minimum criteria defining useful and scientifically accurate information.

Method and findings: Evaluation forms containing the explicit elements that define useful scientifically accurate information for three drugs with known serious adverse drug reactions were created based on the current US FDA approved professional product labels. The Arabic language patient drug information leaflets for celecoxib, paroxetine, and lamotrigine were obtained locally and evaluated using a methodology similar to that used in previous quality content patient drug information studies in the US.

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1. Introduction

The US Food and Drug Administration (US FDA) has said that the distribution of accurate, thorough and understandable information about drugs is necessary to fulfill both a patient’s need and the right to be informed. Regardless of any other effects of such information, the direct educational benefits are sufficient to justify a government requirement that such information be distributed to patients (Department of Health and Human Services, 1995).

A recent *British Medical Journal* editorial commented that “High quality information is essential for good health, yet many individuals, practitioners, and health organizations – particularly in low and middle income countries – lack information” and that the lack of relevant reliable healthcare information should no longer be a major contributor to avoidable death and suffering (Smith and Koehlmoos, 2011). This may also include the lack of useful scientifically accurate drug information for patients.

Access by patients to high quality drug information has a long complex history in the US and is a goal that has not yet been achieved despite the recognition of its potential benefits and the patients’ right to be informed.

1.1. Patient drug information in the US

In 1979, the US FDA proposed regulations that would have required the distribution, by pharmacists, of drug information written specifically for patients. The information would be in a nontechnical language; would not be promotional in tone or content; and would be based on a drug’s approved professional product labeling (Department of Health and Human Services, 1979). The regulations were opposed by pharmacy, medicine, and the pharmaceutical industry (Sasich, 2007). The day after President Reagan’s inauguration in 1981, the White House called the US FDA to make it clear that the patient drug information regulation was not to be enforced. In 1982, US FDA officially canceled the regulation in favor of a plan under which pharmaceutical companies and the private sector drug information publishers would voluntarily make information about drugs available to patients (Pines, 1999).

In the 13 years between the official cancellation of the 1979 regulations and 1995 the US FDA proposed new regulations to ensure that patients received useful scientifically accurate drug information called the Medication Guides for all drugs marketed in the US. During this time the US FDA assessed the quality of patient information leaflets (PILs) produced by commercial drug information vendors including PILs produced by the American Society of Health-Systems Pharmacists, Facts and Comparisons, First Data Bank, and the U.S. Pharmacopoeia. The US FDA found these PILs inadequate. For example, none of the PILs written for enalapril mentioned the contraindications for allergic reactions or angioedema on previous treatment with other angiotensin converting enzyme inhibitors (Department of Health and Human Services, 1995).

The US FDA Medication Guide regulations were followed by the passage of Public Law 104-180 in 1995 that created a public-private process to develop voluntary guidelines that would, in part, define “useful scientifically accurate” drug information leaflets for patients distributed in pharmacies. These guidelines are referred to as the Keystone Criteria. The law required the US FDA to assess the usefulness and scientific accuracy of private sector PILs. This law prevented the US FDA from regulating private sectors’ PILs (Department of Health and Human Services, 1996).

Between 2001 and 2010, four US FDA sponsored evaluations required by Public Law 104-180 assessing the usefulness and scientific accuracy of private sector PILs were published. These evaluations consistently found that private sector PILs failed to meet the accepted definition of useful scientifically accurate PILs as defined in the Keystone Criteria (Svarstad and Mount, 2001; Svarstad et al., 2003a,b; Winterstein et al., 2010).

Regulations finalized in 1998 gave the US FDA the authority to required Medication Guides for a limited number of drugs that were found to present serious public health concerns for which patients should have safety information available that would help in the decision to begin treatment or continue taking a drug (Department of Health and Human Services, 1998). At the present time approximately 200 drugs are required to be dispensed with a Medication Guide in the US.

1.2. Patient drug information – international experience

In 2007, Raynor and colleagues evaluated the quality of PILs provided at the time of dispensing for drugs in the US, UK, and Australia (Raynor et al., 2003). Legislation passed in the European Union (EU) that went into effect on January 1, 1999, required that PILs be written and supplied by a drug’s manufacturer. All contraindications, precautions, and adverse effects in the Summary of Product Characteristics, the EU equivalent of the US professional product label, must be included in the PIL in a form that the patient can understand. In Australia the manufacturer is also responsible for writing the PILs and the content must be consistent with the drugs’...
professional product information and understandable to the patient.

According to Raynor and colleagues, the Australian PILs were generally superior, achieving a level of 90% adherence to the criteria, compared with 81% for the UK leaflets and 68% for those from the US (Raynor et al., 2003).

The original intent of Raynor and colleagues was to evaluate the PILs for four drugs using the US Keystone Criteria in which the definition of useful scientifically accurate information is based on consistency with the US FDA approved professional product label. However, it was found that the information content for the four drugs from three countries was different. The authors subsequently modified the evaluation to accommodate the difference in the information content.

Differences in the information content of professional product labeling have been identified between countries, including between developed and developing countries. The US Office of Technology Assessment (OTA) evaluated a sample of labeling by the US companies in four developing countries. Half the products evaluated had labeling that was entirely appropriate or had relatively small problems. The other half differed significantly and seriously from the US FDA approved professional product labels. Health professionals relying on the information provided with those products could put patients at unnecessary risk; provide less-than-effective treatment, or both. This may occur whenever health professionals are not fully informed about specific dangers of the drugs they are prescribing or recommending, or when they are led to believe that the drug is effective for a condition when effectiveness has not been fully established (US Congress Office of Technology Assessment, 1993).

Important differences in safety warnings for rosiglitazone (Avandia) were found in the prescribing information available in the UK, US, and Saudi Arabia (SA). In general, more complete information was found in the prescribing information available in the UK, US compared to SA. The authors noted that Saudi Arabian prescribers and patients should have access to the most current safety information to guide their decisions about the drugs they are taking (Sasich et al., 2009).

The results from the four US FDA sponsored studies and international experiences prompted our evaluation of the usefulness and scientific accuracy, using the Keystone Criteria definition of Arabic language PILs for three drugs published by a North American commercial drug information vendor. To the best of our knowledge this is the first evaluation of the usefulness and scientific accuracy of native language PILs, including Arabic, that has been reported.

2. Methods

We evaluated the usefulness and scientific accuracy using the Keystone Criteria for Arabic PILs published by Lexi-Comp, Inc. a commercial drug information vendor for the drugs celecoxib, paroxetine, and lamotrigine. The four US FDA sponsored studies selected two and four drugs for evaluation (Svarstad and Mount, 2001; Svarstad et al., 2003a,b; Winterstein et al., 2010) We choose to evaluate three. The three drugs were selected because of their potential to cause serious adverse drug reactions. New prescriptions and refills for all three drugs are required in the US to be dispensed with patient’s Medication Guide.

Evaluation forms were developed for each of the three drugs based on their most recent US FDA approved professional product labels. The most recent revisions of the professional product labels for the three drugs were downloaded from the US National Library of Medicine’s DailyMed website (http://dailymed.nlm.nih.gov). The celecoxib and paroxetine professional labels were revised in April 2011 and the lamotrigine label in November 2010. Exact statements or phrases concerning specific information (explicit elements) were copied from the electronic versions of the drugs US FDA approved professional labels. Two columns were created headed Yes or No for the pharmacist evaluators to indicate whether or not the information was contained in the Arabic PILs.

The celecoxib evaluation form contained 37 explicit elements covering the drug’s box warning; contraindications; warnings and precautions; drug interactions; use during pregnancy and lactation; approved uses; and instructions for patients on recognizing potential adverse reactions and what steps to take should such reactions appear. For example, the statement “increase risk of serious CV thrombotic events, MI, and stroke, which can be fatal” is an explicit element from the celecoxib US professional product label that must appear in the Arabic patient information leaflet as part of the evaluation of useful scientifically accurate information. The evaluation forms for paroxetine and lamotrigine contained 50 and 35 explicit elements, respectively.

The Arabic language PILs for the three drugs were obtained from a large hospital in Doha, Qatar. All of these leaflets had copyright dates of 2011.

The Arabic language PILs were assessed by two experienced bilingual pharmacists, English–Arabic, whose first language is Arabic using the evaluation forms. The pharmacists had to agree yes or no for each explicit element in the drug evaluation forms. An Arabic PIL would have to be 100% consistent with the evaluation form for that drug to be deemed useful and scientifically accurate. The proportion of the information contained in the Arabic leaflets found to be useful and scientifically accurate was also calculated.

3. Results

In this evaluation of the usefulness and scientific accuracy of Arabic language PILs using the US Keystone Criteria as the standard, the PILs for three drugs with known risks of serious adverse events failed to meet the definition of useful and scientifically accurate drug information for patients. The Arabic information for celecoxib contained 30% of the explicit elements defining useful scientifically accurate information. For paroxetine and lamotrigine the results were 24% and 20%, respectively.

The results are summarized in Table 1 below.

4. Discussion

The Keystone Guidelines defined useful scientifically accurate drug information for patients as being consistent with or derived from a drug’s US FDA approved professional product label (Department of Health and Human Services, 1995). The Secretary for Health and Human Services accepted this definition in 1996 for drug information distributed to patients.

Our results assessing the usefulness and scientific accuracy of private sector Arabic PILs are consistent with those reported in previous US and international evaluations of English language PILs. We believe that this is the first systematic evaluation of the information content of Arabic language drug information intended for patients.

Overall our assessment found the same result as the US and international evaluations that none of the three leaflets met the Keystone Criteria guidelines for useful scientifically accurate drug information for patients. However, we found lower proportions of explicit information in the Arabic PILs than was reported for the English language PILs. We believe that this difference is due to differences in the definition of useful and scientifically accurate drug information and in the scope of information evaluated.

In our evaluation of the Arabic PILs the original Keystone Criteria definition and intent for useful and scientifically accurate were strictly followed. We restricted our evaluation to the professional product labeling sections for Indications and Usage; Black Box Warnings; Contraindications; Drug Interactions; use during pregnancy and lactation; and instructions for patients on recognizing potential adverse reactions and what steps to take should such reactions appear. We required that all information listed in these sections of a drug’s professional product labeling be reflected in the Arabic PILs to be scored as being useful and scientifically accurate.

Unlike our evaluation, the Svarstad (Svarstatd and Mount, 2001; Svarstad et al.,2003a,b) and the Winterstein (Winterstein et al., 2010) studies used standards that did not follow the Keystone Criteria strictly. Raynor’s (Raynor et al., 2003) international comparison notes that not all information in a drug’s professional product labeling in Australia needs be in a drug’s PIL. This may account for the lower scores of the Arabic PILs found in our study.

We did not evaluate the formatting and readability of the Arabic language PILs as none of the PILs met the definition of useful and scientific accuracy based on information content.

There is evidence that professional product labeling distributed by multinational pharmaceutical manufacturers to developing countries may contain less information than is available in US FDA approved professional labels (US Congress Office of Technology Assessment, 1993; Sasich et al., 2009). This raises important questions as to establish a standard to evaluate the usefulness and scientific accuracy of PILs.

Our use of the Keystone Criteria for defining useful scientifically accurate patient information can be challenged. Other definitions are possible that could be developed by professional organizations in conjunction with patient groups and the pharmaceutical industry. The Keystone Criteria were chosen as they were developed by a committee that included groups representing patients, commercial drug information vendors, health professionals, and the pharmaceutical industry. Additionally, the Keystone Criteria were accepted by the US government as the standard for patient drug information.

Useful scientifically accurate drug information may be an important but overlooked patient safety intervention. The majority of serious adverse drug reactions are known. A recent study in the US found that most emergency hospitalizations for recognized adverse drug reactions in older adults resulted from a few commonly used medications (Budnitz et al., 2011). Useful scientifically accurate drug information may potentially provide patients the information necessary to avoid or mitigate known adverse drug reactions. This has important implications for individual patients and for costs to healthcare systems.

The Arabic language PILs in our study omitted important risk information. For example, the celecoxib information made no mention of elderly patients and their increased risks of adverse cardiovascular events and gastrointestinal hemorrhage, both potentially fatal. The paroxetine information in Arabic omitted the risk of the use of the drug during pregnancy, which may result in congenital cardiac abnormalities. Notable omissions in the lamotrigine Arabic information were the drug interaction with valproate and the possibility of potentially fatal multiorgan failure.

Incomplete drug information that omits important warnings is potentially misleading that could result in harm if the patient believes that drug information distributed with a drug or by a trusted health professional is all the information that is necessary to use the drug safely and effectively.

There are several limitations to this study. The patient information from only one commercial drug information vendor was evaluated and the evaluation included a limited number of selected drugs. The two bilingual pharmacists’ assessments were not independent. A larger study is needed to include additional vendors, drugs, and independent evaluations by bilingual pharmacist assessors.

5. Conclusions

Health professionals and policy makers that are considering the routine distribution of PILs in their institutions or countries should consider the failure over the past 30 years of private sector commercial drug information vendors to provide useful accurate drug information for patients. PILs written by manufacturers and approved by countries with mature drug regulatory authorities are an option in developed countries. Developing and emerging countries may not have the resources, including experienced staff, to be able to effectively regulate native language PILs. Developing and emerging countries may import drugs from multiple countries with professional product information that varies in content. A possible option for developing and emerging countries is to develop

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<th>Celecoxib</th>
<th>Paroxetine</th>
<th>Lamotrigine</th>
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<tbody>
<tr>
<td>Number of explicit information elements evaluated</td>
<td>37</td>
<td>50</td>
<td>35</td>
</tr>
<tr>
<td>Number of explicit information elements meeting keystone criteria</td>
<td>11</td>
<td>12</td>
<td>7</td>
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<tr>
<td>Percentage adherence to the keystone criteria</td>
<td>30%</td>
<td>24%</td>
<td>20%</td>
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their own human resources and the capabilities to write PILs in their native language using the Keystone Criteria as the standard for useful scientifically accurate drug information.

References


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