Evaluation of clarity and consistency in dosing directions and measuring devices for pediatric over the counter liquid medications used in United Arab Emirates

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The aim of this study was to evaluate the clarity and consistency prevalent in dosing directions and measuring devices used for over the counter (OTC) liquid pediatric medications available in United Arab Emirates (UAE). 130 pediatric oral liquid OTC medications with dosing information for children younger than 12 years were studied. The study specifically focused on issues like the inclusion of a measuring device, child resistance packaging, within product inconsistency between dosing directions on the bottle’s label and dose markings on enclosed measuring device, across-product use of non standard units of measurements and abbreviations, use of numeric text according to the Food and Drug Administration recommendations (FDA) and the presence of definitions for abbreviations used. Out of 130 preparations studied, a measuring device was absent only in 16% (21 products, n=130). 31.5% (41 products, n=130) of the preparations studied did not have the child resistant cap. Dosing directions on the label/leaflet and markings on the measuring device were the same in 53.6% (52 products, n=97) and different in 46% (45 products, n=97) of preparations. Superfluous markings (marking in the dosing device that is not referred to in the product labeled dosage instructions) were present in only 21.5% (23 products, n=107) of the cases. Inconsistent text for units (milliliters) was observed in 41.2% (40 products, n=97) products. Inconsistency in expressing teaspoon and tablespoon (inconsistency in expressing teaspoons as tsps or TSP and tablespoons as tbsp. or TBS) was 18.8% (13 products, n=69) and 28.5% (20 products, n=70), respectively. The use of non standard units, tablespoons and teaspoons needs to be quickly reviewed and prevented in the best interest of pediatric population.

Key words: Over the counter drugs, United Arab Emirates, pharmaceutical preparations, oral drug administration, self administration.

INTRODUCTION

Challenges to pediatric drug therapy include excessive and unnecessary drug use, inappropriate dosage form, inaccurate dosing and improper drug administration (Lawrence, 2009). In November 2009, the Food and
Drug Administration (FDA) released a new set of voluntary guidelines for the industries responsible for producing, selling and distributing the over-the-counter (OTC) medications (FDA, 2009). Several casualties resulting from unintentional overdoses of OTCs in children, which were likely due to the use of these OTC products with confusing labels, inconsistent dosage leaflets and inconsistent measuring devices with ambiguous dosing information, caused the impetus for these new guidelines.

In May 2011, the FDA issued revised guidelines for the production, marketing and distribution of liquid OTC drug products that are measured and dispensed with provided devices such as spoons, cups and droppers (FDA, 2011). The FDA notes that better measuring devices for OTC liquid drug products will help patients in self-administration. Further, parents and other caregivers can administer the right amount of these medications, especially to children. Yin et al. (2010) in New York, Atlanta and Chicago set out to determine the prevalence of inconsistent dosing directions and measuring devices among popular pediatric OTC’s at the time the United States (US) FDA released new voluntary guidelines to industry groups responsible for manufacturing, marketing, or distributing OTC liquid medications, particularly those intended for children. The study concluded that at the time, the FDA released its new guideline, top-selling pediatric OTC liquid medications contained highly variable and inconsistent dosing directions and measuring devices (Yin, 2010).

In March 2009, the United Arab Emirates (UAE) Ministry of Health (Medical Practice and License, 2009; Sharif and Elghandour, 2012) prohibited the use of OTC cough and cold products for children under six-years-old and stated that these medicines should only be prescribed by the physicians. In addition, these products should be dispensed for children of six years and above only by a pharmacist (MOH-RDCD-Policy, 2011).

In October 2011, the Ministry of Health (MOH) reviewed the mode of dispensing of all medications, and listed the majority of cough and cold products as Pharmacist Only Medications (Ph-OM), where a medicine may be supplied without prescription, but must be dispensed by a licensed pharmacist and placed behind the counter (Sharif and Ghandour, 2012).

If there is inconsistency between the measuring device and the dosing instructions, even correct information given by the pharmacist to the consumer may not be sufficient and still a child can suffer from overdose.

The objective of this study was to evaluate the clarity and consistency in dosing directions and measuring devices used for OTC liquid pediatric medications available in UAE. Secondly, we looked at these medications to see if the revised guidelines recommended by the FDA were followed. In addition, the presence of child resistant caps as a means of preventing accidental administration and use of dosing device with only associated product will be evaluated. The findings of this study were compared with those of Yin et al. (2010).

**METHODS**

**Settings and preparations**

130 pediatric oral liquid OTC medications were studied after obtaining permission from the Ethics and Research Committee of Ras Al Khaimah Medical and Health Sciences University. This study was conducted in various pharmacies in the UAE after obtaining the permission from each head of the pharmacy (both out patient and hospital pharmacies).

**Criteria for analysis**

Pediatric OTC medications analyzed in this study were chosen on the basis of the criteria listed in Table 1 and covered medications for allergy, gastrointestinal disorders, analgesics and respiratory disorders (Figure 1).

**Study design**

A descriptive comparative study was conducted using a checklist form which was filled for each OTC preparation, while comparing the dosage device and the leaflet given with it. The features, inclusion of measuring device, presence of child resistance packaging, size of the measuring device in comparison to the largest dose prescribed, within product inconsistency

<table>
<thead>
<tr>
<th>No.</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>1</td>
<td>Liquid pediatric medications to be taken orally</td>
<td>Liquid medication not indicated for oral use</td>
</tr>
<tr>
<td>2</td>
<td>Dosing directions given for a child younger than 12 years</td>
<td>No dosing instructions given for child younger than 12 years</td>
</tr>
<tr>
<td>3</td>
<td>Product selection: OTC liquids used for inflammation, cough/cold (respiratory disorders), allergic or gastrointestinal disturbances</td>
<td>Liquid medications containing vitamins and minerals for oral use</td>
</tr>
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</table>

Table 1. Inclusion and exclusion criteria of OTC medications.
between dosing directions on the bottle’s label/leaflet and dose markings on enclosed measuring device, across-product use of nonstandard units of measurements and abbreviations, use of numeric text (that is, leading zero before a decimal point, use of small numeral font size offset text format [e.g. ½] recommended by the FDA) and presence of abbreviation definitions, presence of elements designed to guide consumers on appropriate use, including: (1) a strategy to ensure that the measuring device is used only with the associated product (e.g. inclusion of written statement or presence of a mechanism to secure the device to its product, such as a dropper that also serves as a cap for the bottle) and (2) a statement warning about appropriate use of the measuring device if the physician’s recommended dose does not match doses marked on the device, were observed and compared between the OTC medications. The features in the form were marked as “present”, “absent” or “non-applicable” in the checklist.

The parameters were observed and compared with findings of the study by Yin et al. (2010) on the basis of guidelines issued by the FDA in 2009 and 2011 for the production, marketing and distribution of liquid OTC drug products that are measured and dispensed with provided devices such as spoons, cups, droppers and the leaflets.

Data analysis

Descriptive analyses were performed for entire data using Microsoft Excel. To compare the significance of the difference in the means of two groups, the Student “t” test was performed, p<0.05 was considered significant.

RESULTS

16.2% (21 products, n=130) of the products lacked dosing device and in 83.8% ([109 products, n=130] (95% CI: 77.8-89.8)) of the products, dosing device was included (Figure 2). Directions should clearly state that the dosing device is meant to be used only with the product with which it is packed. The probability of dosing errors increase when one dosing device is used for another product of different strength. Directions for using the dosing device with only the associated product were provided in 15.4% ([20 products, n=130] (95% CI: 9.1-21.7; p<0.001)) of the products. In 12.3% ([16 products, n=130] (95% CI: 6.6-18)) of the products, the dosing device was larger than the largest dose prescribed which may lead to overdosing. Child resistant packaging was absent in 41 products, (n=130) of the products studied (p<0.001) (Figure 2).

Physicians may tailor the dose as per the body weight or disease condition which occasionally may be different than the usual recommended dose. The dosing device may not have the markings for these revised doses. The packaging should bear warnings for the patient and the caregivers to use appropriate devices in such circumstances. Only 6.2% ([8 products, n=130] (95% CI: 2.0-10.4)) of the bottles and 37.7% ([49 products, n=130] (95% CI: 29.3-46.1)) of the leaflets studied in our survey carried such warnings.

In this present survey, 46.4% (95% CI: 43.5-63.7) of the products in our study showed inconsistency in dosing directions between bottle label and the dose markings on measuring device. Superfluous markings were also observed in 21.5% ([23 products, n= 107] (95% CI: 13.6-29.4; p<0.001)) of the products.

In our study, 41.2% ([40 products, n=97] (95% CI: 31.3 – 51.1)) of the products showed inconsistency in text for units which were expressed as milliliter and in 18.8% ([13 products, n=69] (95% CI: 9.4-28.2)) products, there was inconsistency in expressing teaspoons as tsp or TSP. Similarly, in 28.5% ([20 products, n=70] (95% CI: 17.1-39.2)) of the products tablespoons was expressed as tbsp or TBS (Figure 3).
However in our survey, two products with a dose smaller than one omitted the leading zero, and in one product, the trailing zero was used. International standard units were used in 34.9% [(37 products, n=106) (95%CI: 25.7 – 44.1)] of the products and no product contained atypical units of measurement such as drams, fluid ounces, etc. In 40% (12 products, n=30) of the products in our survey, the tsp abbreviation was defined (Figure 4).

**DISCUSSION**

The developmental differences in gastrointestinal conditions and physiology in the pediatric population may manifest in differences in absorption, distribution, metabolism and excretion of drugs (Ali et al., 2013). Hence, overdose can prove fatal in this already vulnerable population group. Overdosing of OTC medications is estimated to result in emergency hospitalization of 5700 children in USA alone (Yin, 2010). Among many other factors, Yin et al. (2010) in their survey attributed inadequate and inconsistent dosing instructions and measuring device as one of the main causes for these emergencies. Stringent regulatory oversight is necessary to ensure these inconsistencies are minimized. Even though dosing device may be present, yet their use may not be easy or the instructions may not be clear enough.
Figure 4. Units of measurement, use of zeros, abbreviations and fonts.

Dosing devices are provided in the form of cups, syringes, spoons and droppers. A person’s preference for dosing devices (syringes and dosing cups) may vary. In one study, oral dosing syringe was found to have high dosing accuracy (92%) as compared to 85% accuracy when participants used dosing cups (Kay, 2000). Sobhani et al. (2008) in their survey on 96 subjects found that dosing cups were the most commonly used devices and oral syringe was preferred by the 80% of subjects for accurate dose measurement.

No common standard is followed in measurement of pediatric doses. The commonly used units are teaspoons, tablespoons, ounces, milliliters, cubic centimeters, etc. Confusion due to these markings often creates doubt in parents and caregivers mind which may result in overdose or under dose administration. It is estimated that 40 to 60% of parents and caregivers make errors during drug administration to children (Yin, 2010).

To address these concerns, various recommendations are proposed by the FDA guidance document for OTC liquid products (FDA, 2009). The FDA (2009) recommends that all OTC drug products should be accompanied by a measuring device and units of measurements and abbreviations used should be same on the device and in the dosing directions to avoid confusion and dosing errors (FDA, 2009). However, Perrigo (2010) disagreed with the recommendation that device be unique to the associated packaged product. They argued that dosing errors will increase in cases of patients consuming multiple medications.

The guidance further says that no unnecessary markings should be used. Yin et al. (2010) reported 98.6% products with inconsistency between immediate packaging and the dosing device. Since the issuance of FDA guidance document, the inconsistencies have significantly gone down. Comparing the results of Yin et al. (2010) with our findings in UAE, 46% (95% CI: 34.5-53.9) of products had marking inconsistencies between label and the device, that is, the markings described in the label were not consistent with the dosing device. Our studies revealed that 31.5% of products lacked child resistant packaging. Besides being a regulatory requirement, child resistant packaging prevents self administration by children which can be insidious (FDA, 1999).

Muddle between “teaspoon” (tsp) and “Tablespoon” (Tbsp) can easily lead to over-or-under dosing of the medication. Further, these terms tend to give the impression that it is appropriate to use a kitchen spoon as a measurement device. Kitchen spoons are un-calibrated and are not recommended for dosing purpose. However, they are widely used, for example, in one survey Madlon-Kay and Mosch (2000) found that 73% of parents used a kitchen teaspoon to administer medication. As shown in
Table 2. Comparison of inconsistencies in dosing devices in USA and UAE markets.

<table>
<thead>
<tr>
<th>Parameter</th>
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<tbody>
<tr>
<td>Present survey for UAE market</td>
</tr>
<tr>
<td>Standard measuring device</td>
</tr>
<tr>
<td>Inconsistencies between the labeled directions and the dosing device</td>
</tr>
<tr>
<td>Superfluous markings</td>
</tr>
<tr>
<td>Nonstandard units of measurement</td>
</tr>
<tr>
<td>Use of milliliter as unit</td>
</tr>
<tr>
<td>Teaspoon</td>
</tr>
<tr>
<td>Tablespoon</td>
</tr>
<tr>
<td>All abbreviations defined</td>
</tr>
<tr>
<td>Leading zero absent</td>
</tr>
<tr>
<td>No statement mentioning that the measuring device should only be used with the product it is packed with</td>
</tr>
<tr>
<td>On the bottle</td>
</tr>
<tr>
<td>On the leaflet</td>
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Table 2, marked improvement (71.4%) has been made in the expression of tablespoon since Yin et al. (2010) study (18.5%). Smaller font for numerals in fractions as provided in FDA guidelines (2009) was used in all the applicable products (10 products, n=10) surveyed in this study. The supplemental materials accompanying a dosage form must be written at or below sixth-grade reading level and dosing devices should require only one measurement of medication to avoid dosing error (Wallace et al., 2010).

The use of standardized calibrated dosing devices needs to be advocated for reducing dosing errors arising from nonstandard dosing devices. Use of household spoon should be strongly discouraged. The American Academy of Pediatrics recommends using milliliter to enhance standardization and accuracy of dosing instructions (Yin, 2010). Well marked devices will further curtail the unintentional dosing errors. Use of metric units for dosage is also recommended by various other institutes (Official "do not use list" by the joint commission, 2012; United States Pharmacopeial Convention, 2012; Lawrence and Isletts, 2009.). The standardization of dosing devices represents an area for further improvement (Table 2). Identification of dosage and corresponding measure on the label and on the dosing device, respectively, is of paramount importance in the prevention of dosing errors.

To further reduce ambiguity, the FDA recommends the use of one zero before the decimal point (FDA, 2009). The guidance further recommends that zeros should not be used after the decimal point (FDA, 2009).

Though the study by Yin et al. (2010) was conducted in different country with different socioeconomic measure and literacy rate. The comparison provides an insight into the areas which need further improvement. As shown in Table 2, since the inception of the FDA guidance document, significant improvements have taken place in dosing device consistency and uniformity. Further, MOH in UAE has made regulatory oversight stringent which has resulted in significant improvement in therapy.

Significant improvements have been made in terms of reducing the inconsistencies between the labeled directions and the dosing device, reducing superfluous markings, abbreviations, presence of leading zero and in avoiding the use of large font size. However, use of nonstandard units, tablespoons and teaspoons needs to be quickly reviewed and prevented in the best interest of pediatric population.

Conclusion

Absence of child–resistant caps in 31.5% of the syrup products subjects highly vulnerable children population to a high risk of overdose due to accidental ingestion. Different dosing directions were observed on the measuring device and the leaflets of almost half of the medications studied (46.4%). There is an urgent need to further streamline dosing directions and dosing devices to reduce the errors caused by confusion and ambiguities present in existing dosing devices. Replacement of teaspoons and tablespoons with standard units such as "ml" can mitigate the risk caused by inconsistencies in the expression of teaspoons and tablespoons.

REFERENCES


