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Full Length Research Paper

Descriptive study for look-alike and sound-alike medicines based on local language peculiarities

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The existence of confusing drug names was considered one of the leading causes of medication errors. The aim of the study was to summarize the potential sources for errors associated with look-alike and sound-alike (LASA) medicines, to provide overview of the most common patterns and offer recommendations of safety strategies to help mitigate the problem. A standardized questionnaire was conducted for a period of 1 month in 2011. The collected data was statistically analyzed with Microsoft Excel 2007 and SPSS version 17.0. The total of 93 questionnaires was obtained. Two hundred and twenty-three (223) unique LASA drug pairs were identified with prevalence to brand names. The modal Bulgarian brand medicine name had 7 letters, 3 syllables and 1 word. The average generic drug name had 10 letters, 4 syllables and 1 word. The top 15 highest risk-potential pairs from both groups were classified by the values of the Dice coefficient and analyzed by possible impact on prescription and pharmacy practice. The results of the study showed that look-alike medicine names were a possible source of medication errors and threat to patient safety in everyday practice. Safety strategies were needed to reduce the risk of medication errors in community and hospital pharmacies related to LASA drugs.

Key words: Patient safety, medication errors, sound-alike and look-alike drug names.

INTRODUCTION

The processes of discovering, designing, developing, evaluation, marketing authorisation, dispensing and administrating medicines are complex and prone to errors (Cohen, 1999; Corrigan et al., 1999). The existence of confusing the names of medicines is one of the most common causes of prescribing errors and is of concern worldwide (Lambert et al., 1999). Given the large set of existing drug names, the existence of look-alike and sound-alike (LASA) sets of drug names is inevitable. Medical doctors, nurses and pharmacists can get them confused dispensing the wrong one in errors, which can injure or even, be fatal for patients.

One of the main sources of this problem is the large variety of the medicines that are currently on the market under different invented (trade) names but identical International Non-proprietary Names INN). Thus, the (potential for error due to confusing names is significant. Many of the mentioned different names look like other medicines names. There are different types of confusability related to drug names – illegible handwriting, incomplete knowledge of drug names, newly authorized and available on the medicinal products, etc (Lyons, 2008). These factors are inherent to the task of distinguishing drug names, but they contribute to possible medication errors due to LASA drug pairs. It has been demonstrated that similar words compete for recognition with high-usage frequencies competing more than others; this means similar words that are frequent are more likely to generate confusions than similar words that are infrequent (Norris, 1987; Goldinger et al., 1989; Debruille, 1998).

It has also been suggested that the beginning of a word is more important in other parts in listening tasks (Cole, 1973). In language production (spoken or written), words with similar output forms are sometimes confused, and even more common are words both similar in form and similar in meaning (Harley, 1995). Contributing to this

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confusion are the similar clinical use, similar codes in the Anatomical Therapeutic Chemical Classification System (ATC codes) and the failure of manufacturers and regulatory authorities to recognise the potential for error. Regulatory approval process should involve evaluation and conduct rigorous risk assessments for proposed brand names, prior to approving new medicinal products on the market (Hoffman and Proulx, 2003; McCoy, 2005).

There are two types of drug names – INNs and brand or invented or trade marketed names. LASA medicines pairs can be found in both groups.

The World Health Organisation's INNs Expert Group strives to develop INNs for pharmaceutical medicines substances for acceptance worldwide. On the other side, brand names are developed by the pharmaceutical product manufacturer (marketing authorization holder) and often differ between countries. Brand names are approved by regulatory authorities such as the Food and Drug Administration in the United States of America and the Invented Names Review Group in the European Union. However, there are still some brand names that look familiar and may contain different active ingredients in different countries. Regulatory authorities and the pharmaceutical industry have assessed the potential for errors due to confusing names by using computerized screening methods and pre-marketing testing among healthcare professionals. But still, there are new drug names that continue to be approved and are similar to existing ones. This is a reason for occurring medication errors. For example, drug names Zantac® (ranitidine) and Xanax® (alprazolam) are problematic in many countries (Lambert et al., 1999).

The problem of look-alike medicine names leads to research for development of different regulatory and safety strategies to prevent medication errors. Although, different factors have implications for predicting confusing drug names, we focus on LASA similarity as a source of possible medication errors. The aim of the study is to summarize the possible errors associated with LASA medicines. We investigate the most common patterns observed in Bulgaria and offer recommendations for regulatory strategies to help mitigate the problem.

MATERIALS AND METHODS

Phonetic versus orthographic methods

The approaches to measuring word similarities can be divided into two groups. The orthographic approaches disregard the fact that alphabetic symbols express actual sounds focusing on character comparison. The phonetic approaches, on the other hand, attempt to take advantage of the phonetic characteristics of individual sounds in order to estimate their similarity.

To explain the method for examining the similarity between the defined drug pairs, we chose to clarify some linguistic characteristics of the Bulgarian language. In Bulgarian, all the letters in a word correspond to vocal sounds or in other words "what is seen is what is to be read". This is the reason why there is no difference between the LASA drug pairs, respectively the phonetic and orthographic approach in Bulgarian, and further we will relate to them as LASA drug pairs.

Sample size selection

In 2011, the number of pharmacists with master degree in Sofia, Bulgaria was 1800 (Bulgarian Pharmaceutical Union website, 2011). In order to determine the size of the sample, the Statcalc module of the Epi Info software was used (Dean et al., 2011). At 95% confidence level, a confidence interval of 8%, the size of the sample is calculated to be 139 people. The sample size was increased with 5% up to 146 people so that possible drop-outs and invalid questionnaires could be compensated. To improve the sample precision, there was equal distribution between community and hospital pharmacists (75 community and 75 hospital pharmacists) due to the difference in the products they work with. The only inclusion criterion in the study was that the respondent should have master degree in pharmacy and professional authorization to practice.

We used questionnaire as a voluntary direct anonymous standardized survey. The validation of the questionnaire was performed in December, 2010 with a test phase including 5 pharmacists. For a month (January and November, 2011), each participant was asked to name five LASA drug pairs either INNs or brand names. The main outcome measures were lengths of drug names, number of syllables, string similarity (Dice coefficient).

The defined LASA drug pairs were examined by string similarity and edit distance. String similarity measures estimate the similarity between two strings based on the number of characters they have in common. Edit distance measures count the number of steps required to transform one string into the other. As both measures can be used for either of the two classes of sting matching (orthographic or phonetic), we considered them appropriate for the objective of our research.

Similarity

The phonological similarity between INN LASA pairs and brand-name LASA pairs was examined by breaking down the words into 3-letter subsequence of adjacent letters (trigrams) and then examining the common trigrams in between the 2 words in the pair. To accomplish this, the unique trigrams in each name were generated. For example, for the drug Klacid® the unique trigrams were {--k, -kl, kla, lac, aci, cid}. In this case, two spaces were added to the beginning of each word to increase sensitivity to similarity at the beginning of words (Lambert et al., 1999). For the drug Klacar®, the unique trigrams were {--k, -kl, kla, lac, aca, car}. Trigram string similarity was defined by the Dice coefficient:

$$S = 2C / [A+B]$$

Where: A is the number of unique trigrams in the first word, B is the number of unique trigrams in the second word, and C is the number of common trigrams between the two words

The trigram string similarity between Klacid® and Klacar® is [2*4] / [6+6] = 0.66667.

Each pair of the brand-name and INN LASA medicines was analyzed for trigram string similarity.

The collected questionnaires were analyzed by SPPS v.17.0 (IBM, 2008) and Microsoft Excel 2007.

RESULTS

A total of 93 questionnaires were obtained (response

Table 1a. Descriptive statistics for brand names of medicines.

Brand names			
Descriptive statistics	**Number of letters**	**Number of syllables**	**Number of words**
N	305	305	305
Mean	7.49	3.00	1.03
Standard error of mean	0.089	0.037	0.010
Median	7.00	3.00	1.00
Mode	7	3	1
Standard deviation	1.550	0.641	0.178
Minimum	4	1	1
Maximum	13	5	2
Sum	2285	914	315

Table 1b. Descriptive statistics for INN names.

INNs			
Descriptive statistics	**Number of letters**	**Number of syllables**	**Number of words**
N	82	82	82
Mean	10.06	3.95	1.00
Standard error of mean	0.173	0.087	0.000
Median	10,00	4.00	1.00
Mode	10	4	1
Standard deviation	1.566	0.784	0.000
Minimum	7	3	1
Maximum	14	9	1
Sum	825	324	82

rate 62%). During validation and preliminary analysis, the repeating LASA INN and brand pairs were removed. The participants pointed a total number of 176 brand-names look-alike pairs and 47 INN look-alike pairs. The prevalence of the first can be explained by the fact that in Bulgaria generic substitution is not allowed without prescribers' approval and not a real practice. The pharmacists perceived INN LASA pairs as a smaller thread for medication errors as a whole.

The obtained medicines names were divided in two groups: INNs and INN LASA pairs and brand names and brand LASA pairs. Both INNs and brand names were analyzed by length, number of syllables and number of words (Tables 1a and 1b).

Tables 1a and 1b provided basic descriptive statistics for the two groups we analyzed. The modal Bulgarian medicine name had 7 letters, 3 syllables and 1 word. In comparison, the INN names had more letters and more syllables.

The top 15 highest results for both groups are shown in Tables 2a and 2b. The first five pairs by values of Dice coefficient were analyzed by edit distance. Edit distance refers to the number of edits [deletions, insertions and substitutions] required to transform 1 word into another. The results showed that the highest values were for the pairs carvedil-carvedilol, finalgel-finalgon, medoclav-medoclor and hexamidine-hexatidine (edit distance is 2).

DISCUSSION

As the results of the study show, the top 15 LASA names in both groups have a Dice coefficient above 0.5. For the purpose of the analysis and because of the nature of Bulgarian language (Cyrillic and phonetic), we accept to assume that Dice coefficient values equal or higher to 0.5 are a predisposition to medication and dispensing errors. The higher values of the coefficient in the brand names group suggest a bigger chance for confusion. The top LASA INN drug names include medicines from different therapeutic groups such as widely used corticosteroids (betamethasone/beclomethasone), non-steroidal anti-inflammatory drugs (ketoprofen), calcium antagonists (lacidipine) and vinca alkaloids (vinblastine/vincristine). The highest chance for possible medication error is observed in those pairs formed by representatives of different therapeutic classes (ketoprofen/ketotifen; cinnarizin/cetirizine; dobutamine/dopamine).

Table 2a. Top 15 LASA brand names of medicines.

Brand LASA pair		Dice coefficient
Carvedil	Carvedilol	0.888888889
Finalgel	Finalgon	0.75
Medoclav	Medoclor	0.75
Calgel	Calgevax	0.714285714
Normodipine	Normodiab	0.7
Esberitox	Esbericum	0.666666667
Klacid	Klacar	0.666666667
Maxidex	Maxipime	0.666666667
Medrin	Medrol	0.666666667
Pentasa	Pentaxim	0.666666667
Spasmo-Lyt	Spasmomen	0.666666667
Dactarin	Daktacort	0.625
Macropen	Macrotec	0.625
Octanate	Octanine	0.625
Pyramem	Pyranthel	0.625

Table 2b. List of top 15 LASA INN names.

INN LASA pair		Dice coefficient
Prednisone	Prednisolone	0.818181818
Calcipotriol	Calcitriol	0.727272727
Hexamidine	Hexatidine	0.7
Betamethasone	Beclomethasone	0.666666667
Heparin	Heparoid	0.666666667
Pyridoxine	Pirenoxine	0.6
Dobutamine	Dopamine	0.555555556
Carboplatin	Carboprost	0.545454545
Glipizide	Gliclazide	0.526315789
Ketoprofen	Ketotifen	0.526315789
Ribavirin	Riboflavin	0.526315789
Lacidipine	Lecarnidipine	0.52173913
Chlorphenamine	Chlorpromazine	0.5
Cinnarizin	Cetirizine	0.5
Vinblastine	Vincristine	0.454545455

Regulatory and safety strategies

The large number of look-alike medicines names requires the adoption of different regulatory and safety strategies in order to prevent and decrease medication and prescription errors due to similar names. Some of the strategies are:

1) Obligatory adoption of two red/blue lines signs on the packages of medicinal product which contain controlled substances (narcotics) – completed in Bulgaria with the special law and delegated acts from the year of 1999;
2) Narcotic substances are to be stored separately– adopted in pharmacy practice many years ago;
3) Implementation of TALLman letters in the look-alike invented names – this technique should be implemented for identifying medications, not only on pharmaceutical industry labels, but also in other places where drug names appear, including computerized prescription software, pharmacy system screens, automating dispensing cabinet screens, labels for pharmacy preparation and shelves, etc (Otero Lopez et al., 2012);
4) Avoidance of any abbreviations;
5) Regulatory measures and rules toward brand names;
6) Generic and brand names are to be printed on unidose packaging;
7) ATC codes to be printed on packaging;
8) Look-alike auxiliary alerts on medication storage bins;
9) Storing medications in non-alphabetic order;
10) Limitation of verbal/telephone orders (especially for hospital pharmacies);
11) Maintaining public accessible list of LASA medications to include “real time” review of new medications (McCoy, 2005)

The large variety of look-alike medicines names on the market is a predisposition for medication errors both during prescription process and pharmacy practice. The large impact of interactive advertising could create confusion among patients (Jimenez et al., 2011). All healthcare professionals should be educated and alerted for the possibility of confusion and adopt different safety strategies to prevent errors in their practice. Proposals for practical steps and effectiveness assessment should be part of our post-marketing surveillance in the future.

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