UNIVERSITAT DE BARCELONA

Seguridad del paciente: estudio de factores para su consecución

Carlos de Figueiredo Escribá

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9.- DIFUSION

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Autores:	Modamio P , **Figueiredo C**, Lastra CF, Mariño EL.
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PREVENTABLE MEDICATION ERRORS INVOLVING LOOK-ALIKE/SOUND-ALIKE MEDICINE NAMES AND SIMILARITIES IN PACKAGING APPEARANCE: TRAINING THE FUTURE PHARMACISTS FROM DIRECT EXPERIENCE

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Background:

Confusion caused by Look-Alike/Sound-Alike (LASA) medicine names and similarities in packaging appearance is a well-known source of medication error (ME) all over the world. Training future health care professionals is an important strategy towards preventing ME.

Purpose of Study:

To analyse reporting of preventable medication errors involving Look-Alike/Sound-Alike (LASA) medicine names and similarities in packaging appearance by pharmacy students in order to highlight the importance of their future role in error prevention and patient safety.

Study Design and Methods:

- The ME were detected and reported by pharmacy students in the course "Clinical Pharmacy and Pharmaceutical Care" (fourth year, second semester of the pharmacy syllabus), from their own and direct experience (at home, friends, etc.).
- Reporting method: voluntary through the Medication Safety Reporting Program (SEGURMED) available at our website.
- Reporting period: three months (March-May 2014).

Findings of Study:

Reports: 505 from 193 students, resulting in 375 accepted and 87 refused (1.9 accepted errors per student).

From the total accepted errors, 128 (34.1%) involved unsafe medicines naming - Brand names and International Nonproprietary Names (INN) - and packaging.

Error categories: Classified into 4 main sets:

(1) Look-Alike packaging and same drug (66.4%)

(2) Look-Alike packaging but different drug (23.4%). There was found a set of LASA drug names and Look-Alike packaging at the same time (n=7, 5.6%)

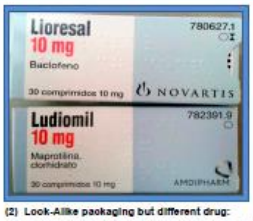
(3) Look-Alike/Sound-Alike brand name (8.6%)

(4) Look-Alike/Sound-Alike drug name (2.3%)

Category of the error: Most of them (n=125, 96.7%) were considered potential ME (category A). Just 3 out of 128 (2.3%) were considered ME (concretely, dispensing errors related to LA packaging that occurred in community pharmacy), although these did not cause harm to the patient (category B).

We must note that one of this ME observed happened while using an electronic prescription order, which is considered one of the strategies for avoiding these kinds of errors.

(1) **Look-Alike packaging and same drug:** *Diazepam Prodes 10 mg vs. Diazepam Prodes 5 mg* (INN: Diazepam).



(2) **Look-Alike packaging but different drug:** *Lioresal 10 mg* (INN: Baclofen) *vs. Ludiomil 10 mg* (INN: Maprotiline hydrochloride).

(3) **Look-Alike/Sound-Alike brand name:** *Drosure diario 0.03 mg/ 3 mg comprimidos recubiertos con película EFG vs. Drosurelle diario 0.02 mg/ 3 mg comprimidos recubiertos con película EFG* (INN: Drospirenone, Ethinyl Estradiol).

(4) **Look-Alike/Sound-Alike drug name:** *Ketoprofeno 200 mg comprimidos de liberación prolongada* (INN: Ketoprofen) *vs. Ketoconazol 200 mg comprimidos* (INN: Ketoconazole).

Example of Medication Error category B: *Risperidona MYLAN 3 mg comprimidos recubiertos con película EFG vs. Risperidona MYLAN 2 mg comprimidos EFG* (INN: Risperidone).

Examples of different dosage forms: *Fluoxetina CINFA 20 mg cápsulas duras EFG vs. Fluoxetina CINFA 20 mg comprimidos dispersables EFG* (INN: Fluxetine; hard capsules vs. dispersable tablets); *Ebastina TEVA 10 mg comprimidos recubiertos con película EFG vs. Ebastina TEVA comprimidos bucodispersables EFG* (INN: Ebastine; dosage form: Covered film tablets vs. bucodispersable tablets).

Conclusions :

Look-Alike packaging was found to be the main contributing factor for potential ME found by pharmacy students. In order to bring attention to this situation it is important to establish a clear classification and point out the complexity of this problem. Working with future pharmacists from their direct experience will help establish new approaches to aid in abolishing preventable ME in our country.

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Error de medicación por similitud ortográfica. Aproximación algorítmica.

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1.- Introducción

En numerosos estudios se ha identificado la similitud de nombres de los medicamentos como una importante fuente de errores de medicación (EM) [1,2]. Esto ha hecho que diferentes grupos de investigación hayan trabajado y estén trabajando en la búsqueda de soluciones para minimizar el impacto de esta situación.

Así, diversos organismos oficiales responsables de la aprobación de los nuevos medicamentos y, por lo tanto, de sus nombres han establecido sistemas más o menos complejos para evaluar la similitud de un nuevo nombre propuesto en relación a los que ya existen en el mercado. Por ejemplo, la FDA ha establecido el Phonetic Orthographic Computer Analysis Software (POCA) para la revisión de los nombres comerciales de medicamentos [3]. Este sistema utiliza algoritmos complejos para identificar potenciales nombres similares, teniendo en cuenta aspectos tanto ortográficos como fonéticos, que ayudan a aprobar o no las propuestas de nombres comerciales de nuevos medicamentos presentadas [4,5].

No se conoce, sin embargo, ningún sistema similar al POCA de la FDA, ni se ha encontrado en la bibliografía ningún estudio sobre la situación de los nombres de los medicamentos en el mercado español utilizando algún tipo de aproximación algorítmica. Por ello, el objetivo principal del estudio ha sido establecer un grupo de algoritmos matemáticos, que ayuden a identificar y, en su caso, predecir potenciales confusiones en los nombres de los medicamentos comercializados en España.

2.- Material y Métodos

2.1.- Selección de la muestra

Los nombres de los medicamentos utilizados para el estudio se distribuyeron en dos grupos formados por 454 parejas de nombres. El primero estaba formado por aquellas consideradas como posible fuente de confusión [6,7], denominándose grupo similar. El segundo formado por parejas de nombres no incluidas en el primer grupo, constituyendo un grupo que se denominó control.

2.2.- Algoritmos aplicados

Se identificaron en la bibliografía diferentes algoritmos, seleccionándose algunos que han sido utilizados en estudios similares [8,9,10], entre ellos los basados en la distancia de Edición (EDR y NED), los que utilizan la Fórmula de Dice (BIGRAM, BIGRAM1B, TRIGRAM y TRIGRAM2B) y los basados en la longitud de la subsecuencia común mayor entre las dos cadenas (LCSR1 y LCSR2).

2.3.- Tratamiento estadístico de los datos

Para establecer la existencia o no de diferencias estadísticamente significativas entre ambos grupos se aplicó el test ji-cuadrado, calculándose la v de Cramèr para medir la intensidad de dicha asociación.

3.- Resultados y Discusión

Tras la aplicación de los ocho algoritmos se pudo apreciar que existían diferencias en los resultados obtenidos para cada uno de los dos grupos analizados. En las Figuras 1 y 2 se muestran, a modo de ejemplo, los resultados obtenidos tras la aplicación de los algoritmos EDR y LCSR1.

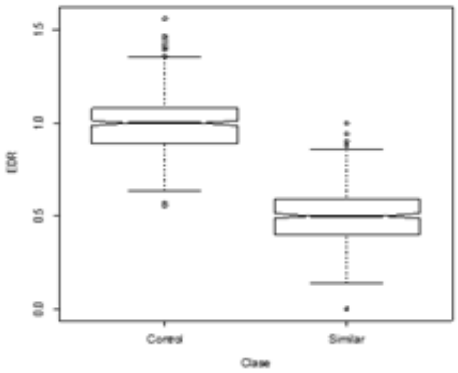

Figura 1.- Gráfico de cajas del algoritmo EDR

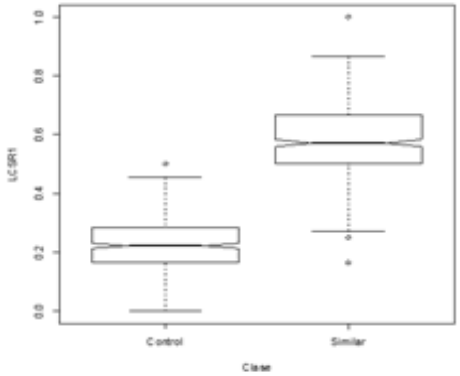

Figura 2.- Gráfico de cajas del algoritmo LCSR1

Así mismo, los resultados de cada algoritmo al aplicar el test de ji-cuadrado demostraron que estas diferencias eran estadísticamente significativas entre los dos grupos, similar y control, con valores de p inferiores a 0,001 en todos los casos, como se aprecia en la tabla 1:

Algoritmo	χ^2	p	V de Cramèr
EDR	742,626	<0,001	0,904
NED	714,966	<0,001	0,887
BIGRAM	521,890	<0,001	0,758
BIGRAM1B	669,216	<0,001	0,858
TRIGRAM	669,216	<0,001	0,858
TRIGRAM2B	685,260	<0,001	0,869
LCSR1	723,392	<0,001	0,893
LCSR2	726,192	<0,001	0,894

Tabla 1.- Resultados del test ji-cuadradopor algoritmo

4.- Conclusiones

Los algoritmos utilizados en el presente estudio diferencian las parejas de nombres de medicamentos incluidas en el grupo de similares de las del grupo control, indicando que podrían ser una herramienta útil en la identificación de posibles confusiones entre nombres de medicamentos en el mercado español.

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Medication Error Due to Drug Name Similarity: An algorithmic approach to Orthographic Similarity

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***SUMMARY*. Numerous studies have identified drug name similarity as a significant source of medication error. One of the approaches employed to minimise this problem has been to apply algorithms designed to act on strings of letters. Two sets of Spanish drug name pairs were used. Eight algorithms reported in the literature were applied to establish the degree of similarity between the different names. Statistical methods were used to assess algorithm performance. The main element of analysis was V of Cramer. Simple mathematical and logical operations were applied to the algorithms in order to enhance differences between the two sets of drug name pairs studied and thus optimise the final results. The results confirm that the algorithms differentiated between the two sets of drug names, indicating that they could serve as a useful tool to identify potential confusion between drug names that could lead to medication errors.**

RESUMEN. Numerosos estudios han identificado la similitud del nombre del medicamento como una fuente importante de error de medicación. Uno de los enfoques empleados para minimizar este problema ha sido aplicar algoritmos diseñados para actuar sobre cadenas de letras. Se utilizaron dos grupos de parejas de nombres de medicamentos españoles y se aplicaron ocho algoritmos reportados en la literatura para establecer el grado de similitud entre los diferentes nombres. Se utilizaron métodos estadísticos para evaluar el rendimiento del algoritmo. El principal elemento de análisis fue la V de Cramer. Se aplicaron operaciones matemáticas y lógicas simples a los algoritmos para mejorar las diferencias entre los dos grupos de pares de nombres de medicamentos estudiados y así optimizar los resultados finales. Los resultados confirman que los algoritmos diferenciaron entre los dos grupos de nombres, lo que indica que podrían servir como una herramienta útil para identificar posibles confusiones entre los nombres de medicamentos que podrían dar lugar a errores de medicación.

INTRODUCTION

Since the publication of *To Err is Human: Building a Safer Health System* by the Institute of Medicine (IOM) [1] and *Building a Safer NHS for Patients: Improving Medication Safety* published by the UK National Health Service [2], several studies have reported the increasingly important role played by health professionals in identifying, preventing and reducing medication errors (ME) and thereby improving the safety and quality of patient [3,4].

There is widespread consensus that the high frequency of adverse events associated with drugs as a result of ME is unacceptable, and that one of the causes of ME is phonetic and orthographic similarity between drug names. Poor handwriting on a handwritten prescription, orthographic similarity on an electronic prescription, incorrect pronunciation when dispensing and erroneous administration because of similar packaging and/or names may all lead to ME at any point in the drug use chain, with possible negative outcomes [4-9]. It is important to point out that not only the prescription but all the drug use chain is involved in the problem even in the drug administration at home.

The US Pharmacopoeia (USP) registered a total of 26,604 spontaneous reports of errors due to orthographic and/or phonetic similarity for the period 2003-2006. An analysis of those errors identified 3,170 pairs of drug names that had produced confusion, and in 1.4% of cases

KEY WORDS: algorithm, look-alike drug names, medication error.

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had caused harm to the patient [10,11]. Observational studies have suggested that the ratio of ME due to these causes is 0.1‰ of all prescriptions dispensed in the US [12]. Given the volume of medications dispensed, even a low rate of drug distribution process translates into a large number of errors [13,14]. Furthermore, up to 25% of ME reported to the USP-ISMP Medication reporting Program involved pair of drugs whose names look or sound alike [15]. Thus, orthographic or phonetic similarity clearly has a fundamental impact on the occurrence of ME; however, no definitive solutions have been proposed to date [16,17]. It is evident that much remains to be studied and improved in this field in order to determine the real magnitude of the problem and measure the impact of present and future initiatives aimed at minimising it [5,18-23].

Some government agencies responsible for approving new drugs, and therefore their names, have developed systems of varying complexity to assess the similarity of a proposed new name to those of drugs already on the market. For example, the FDA has established the Phonetic Orthographic Computer Analysis (POCA) software program to review proprietary drug names, as announced in the Federal Register of the US Government [24]. This system forms part of the Division of Medication Error Prevention and Analysis (DMEPA) and uses complex algorithms that take both orthographic and phonetic aspects into account to identify potentially similar names [25,26], as well as other tools that help determine whether or not to approve the proprietary names for new drugs proposed by laboratories that hold marketing authorisation [26].

In addition, different studies have been conducted on this algorithm-based approach with the common aim of applying algorithms to prevent ME due to orthographic or phonetic similarity [27-29]. In Spain, the Spanish Agency of Medicines and Medical Devices (SAMMD) is responsible for ensuring the quality, safety, efficacy and the veracity of the information authorized medicinal products, published guidelines for drug name approval [30] which outline current legislation concerning the conditions that new drug names must fulfil in order to gain authorisation. However, there is no system in Spain similar to that of the FDA's POCA program, nor have we been able to identify any studies in the literature that use an algorithm-based approach to analyse drug names. Even more, in the introduction of the SAMMD document [30], it is point out that taking in consideration the varieties of languages in the European Union, the name of drugs (brand name) marketed in Spain is under the competencies of the SAMMD for safety reason. Therefore, the Agency could change the drug name if necessary.

In June 2015, the SAMMD register 21,753 different medicines [31], with around 4,000 different brand/drug names. Meanwhile, according to data from IMS Health, more than 720 million prescriptions were issued between April 2014 and March 2015, and almost 1,328 million packages of prescribed drugs were dispensed. This indicates the potential number of ME due to orthographic and/or phonetic similarity of names and the need for ways to minimise the problem. Furthermore, close to 20% of the names reported as source of error were generic drugs [17,32].

The main aim of this study was therefore to establish an algorithm, or group of algorithms, that would help identify, and where appropriate predict, potential confusion over the names of drugs marketed in Spanish. The algorithm or algorithms were required to achieve high values (above 95%) of sensitivity and specificity.

MATERIALS AND METHODS

Selection of the drug name sample

The drug names used to test the algorithms were divided into two sets, one of which comprised pairs of problem names that had been reported as a source of error and was termed "Similar", while the other consisted of pairs that were not known to have caused errors, and was called "Control".

The inclusion criterion for the first set of pairs of similar drug names was having been reported from hospital pharmacy services or community pharmacies. This information was obtained from Spanish databases [17,32] than yielded 454 pairs of drug names that had been reported as a source of error due to drug name similarity. Hospital pharmacy services and community pharmacies voluntarily communicate detected error though a form available for this [17].

The Control set was constructed with 454 pairs of drug names selected at random, ensuring that these did not appear in the previous set of pairs of names.

Algorithms applied

The algorithms applied to measure orthographic similarity that have been used in studies in other countries such as the US or Canada [27,29,33].

They include three distinct groups: those based on the edit distance (ED), also known as the Levenshtein distance; those that use the Dice formula, which can be called n-gram algorithms; and those based on the length of the longest common subsequence (LCS) in the two strings.

In the first group, the ED indicates the minimum number of operations required to transform one string into another [29,33,34], where operation is understood to mean the insertion, deletion or substitution of a letter, and has a value that is given by a natural number. Two algorithms from this group were used. The first, the Normalised Edit Distance (NED) [28,33,34], is obtained by dividing ED by the number of letters in the longest string being compared, *i.e.* the longer of the two names. Second, a variant of the first was proposed, the Edit Distance Ratio (EDR), which is obtained by dividing ED by the mean length of the strings being compared. Thus, if two strings are compared (in our case, two drug names: A and B), the EDR is given by the edit distance between A and B divided by the mean number of letters in A and B.

The second group of algorithms, called n-gram algorithms, contains algorithms based on comparing two strings in sets of n letters. For example, BIGRAM compares the coincidence of letters between words in strings of 2 letters, TRIGRAM in strings of 3, and so on [29]. The value of this algorithm comes from the Dice formula (Eq. [**1**]:

$$\frac{2\ x\ tBA}{Len(A)\ +\ Len(B)} \qquad [1]$$

where *tBA* is the number of coincidences in n letters between the two strings compared.

Four algorithms were selected from this group: BIGRAM, TRIGRAM, BIGRAM1B and TRIGRAM2B [28,29]. The latter two insert one and two blank spaces, respectively, at the beginning of each of the strings. If the drug names have the same first letter, the latter two algorithms highlight this coincidence, whereas the other algorithms in this group do not. TRIGRAM2B prioritises the first pair of letters.

Finally, two algorithms were selected from the last group which are based on calculating the length of the LCS [29,33,35]. One is obtained by dividing the LCS by the number of letters in the longest string being compared (LCSR1) [29,33,35]; the other algorithm proposed, calculated a value by dividing the LCS by the average length of the drug names [33] (LCSR2), similar to the procedure for algorithms using the ED.

Statistical data analysis

Excel 2013 was used to apply the algorithms to the pairs from the Similar and Control sets, having programmed each of the algorithms required in Visual Basic for Applications (VBA) [36]. Statistical analysis was conducted using the statistical package R, which is a software environment for statistical computing analysis and graphcs [37].

Once the algorithms had been applied, the Kolmogorov-Smirnov test was used to assess normality. Whether there was normality in both sets or not were used parametric or nonparametric statistical tests. Where an algorithm presented significant differences, the value range for each algorithm that indicated differences for the two sets was divided into 11 equal intervals so that each range was assigned the number of name pairs per set. The nonparametric chi-squared test determined the existence of an association between sets and obtained V of Cramer to measure the intensity of the association. In each case, the sensitivity and specificity of each algorithm was calculated for each cut-off point.

Sensitivity was calculated using Eq. [**2**]:

$$S = \frac{TP}{TP+FN} \times 100 \qquad [2]$$

Specificity was defined by Eq. [**3**]:

$$E = \frac{TN}{TN+FP} \times 100 \qquad [3]$$

where *TP* are the true positives, *i.e.* pairs from the Similar set identified as similar, *TN* are the true negatives, *i.e.* pairs from the Control set identified as different, *FN* are pairs from the Similar set identified as different and *FP* are pairs from the Control set identified as similar.

Should none of the algorithms obtain sensitivity and specificity values greater than 95%, groups of algorithms, *i.e.* complex algorithms would be considered.

RESULTS

The eight algorithms described above were applied to the two sets of 454 drug name pairs yielded the corresponding values for each pair and algorithm. Fig. 1 shows three different algorithms box plots by group: EDR, TRIGRAM2B and LCSR1.

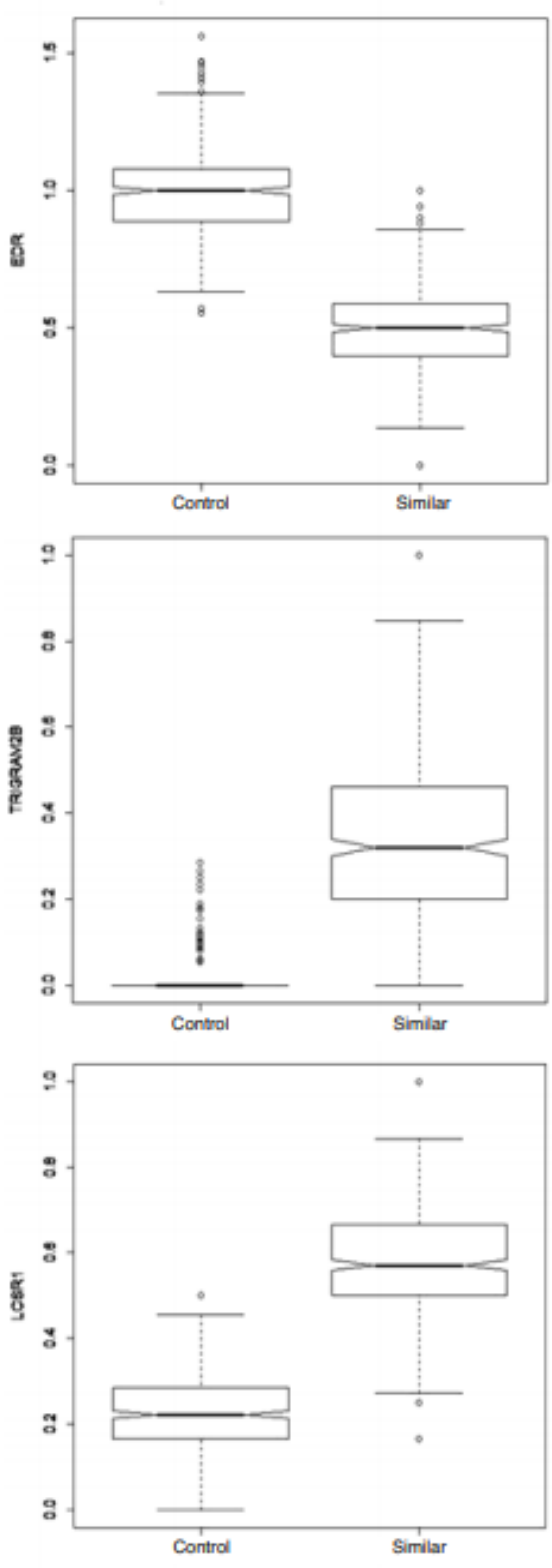

Figure 1. EDR, TRIGRAM2B and LCSR1 Box Plots by Group.

First, a Kolmogorov-Smirnov test was performed to determine the normality of the sets resulting from application of the algorithms. Normal distribution was not found for any of the algorithms in the two groups simultaneously.

Then, the Similar and Control sets were compared using the nonparametric Mann-Whitney U-test showing statistically significant differences between the two sets ($p < 0.001$).

Next, the value range of each algorithm for the two sets was divided into 11 equal intervals, each of which was assigned the number of drug pair names, distinguishing the set from which they came. Applying the chi-squared test again was evidenced differences between the two sets.

Then, different cut-off points in algorithm values were studied to accurately identify whether they defined the pair of drug names as belonging to the Similar or Control set. The algorithm cut-off points were also used to calculate the sensitivity and specificity of each test (Table 1). As can be seen 95% values of sensibility and specificity were not reached at the same time.

At this point, it was tried to use multinomial logistic regression with the algorithms, trying to find better results, but the system does not adjust properly, giving each coefficient of the regression too high standard deviations.

The algorithms that use ED yielded lower values for similar pairs, as was to be expected since they analyse differences between strings. However, those that emphasise the similarity of strings, as in the case of n-gram and LCS-based algorithms, gave higher values to pairs that could give rise to confusion.

It was therefore decided to establish an algorithm that combined both features in order to increase the differences between sets. Following a study of different algorithms, a further group was formed that highlighted these differences. These complex algorithms were: EDR – TRIGRAM2B, NED – TRIGRAM2B, LCSR1 + TRIGRAM2B – NED, TRIGRAM2B – 2xEDR, LCSR1 + TRIGRAM2B – 2xEDR, EDR + NED – TRIGRAM2B, LCSR2 + TRIGRAM2B – 2xEDR, LCSR1 + TRIGRAM2B – EDR – NED and LCSR1 + TRIGRAM2B – 2xNED.

As before, the Kolmogorov-Smirnov test of normality was applied to each algorithm, revealing that none of the algorithms presented a normal distribution. Next, the Mann-Whitney U-test

Algorithm	Cut-off	Sensitivity	Specificity	χ^2	p-value	V of Cramer
EDR	< 0.7102	91.2%	96.7%	703.459	<0.001	0.880
	< 0.8522	98.2%	84.6%	634.638	<0.001	0.836
NED	< 0.6363	89.2%	95.6%	655.649	<0.001	0.850
	< 0.7272	95.8%	89.7%	665.722	<0.001	0.856
BIGRAM	> 0.1590	80.6%	90.1%	458.034	<0.001	0.710
	> 0.2386	70.7%	96.5%	438.955	<0.001	0.695
BIGRAM1B	> 0.1590	91.4%	89.9%	599.971	<0.001	0.813
	> 0.2386	83.0%	96.7%	588.257	<0.001	0.805
TRIGRAM	> 0.0681	63.7%	95.2%	348.637	<0.001	0.620
	> 0.1363	49.8%	99.3%	290.396	<0.001	0.566
TRIGRAM2B	> 0.0909	94.7%	89.9%	651.115	<0.001	0.847
	> 0.1818	77.3%	98.2%	542.010	<0.001	0.773
LCSR1	> 0.3636	96.3%	88.6%	656.878	<0.001	0.851
	> 0.4545	84.6%	98.5%	638.412	<0.001	0.839
LCSR2	> 0.3636	98.2%	83.5%	619.848	<0.001	0.826
	> 0.4545	90.8%	95.8%	682.143	<0.001	0.867

Table 1. Chi-squared Test. Possible cut-off points.

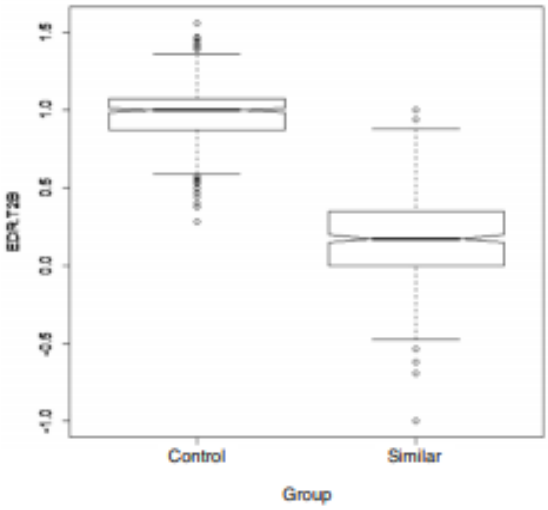

Figure 2. EDR - TRIGRAM2B Box Plot by Group.

for unpaired data with a continuity correction was applied to determine whether the groups presented statistically significant differences in distribution ($p < 0.001$). Box plot for the EDR – TRIGRAM2B complex algorithm are presented in Fig. 2, there is possible to appreciate how this complex algorithm improves to simple ones.

Optimal cut-off points for each algorithm were sought in order to maximise the intensity of association, *i.e.* seeking the highest V of Cramer possible, using the same method applied previously. The results are given in Table 2.

Finally, the complex algorithms were applied to the almost all the different drug names in the Spanish market in April 2016 [38], around 4000 drug names, trying to see how the system worked in a big sample of different pairs of drug names. This study confirm that the system works for great samples improving the specificity in almost all the mixed algorithms.

DISCUSSION

The results obtained confirm that the eight algorithms tested differentiated between the two sets of drug pair names, indicating that they could serve as useful tools to identify potential confusion or error between drug names.

Each of the algorithms yielded a sensitivity or specificity value greater than 95%, but in no case was this value obtained for both parameters at the same time. In contrast, differentiation between the sets was improved when complex algorithms were used since these acted on opposing parameters, thereby yielding better results than when using individual algorithms, and thus exceeding the 95% value required for both sensitivity and specificity in all of them but one.

Algorithm	Cut-off	Sensitivity	Specificity	χ^2	p-value	V of Cramer
EDR - TRIGRAM2B	< 0.670	97.1%	94.9%	770083	< 0.001	0.921
NED - TRIGRAM2B	< 0.600	96.0%	95.4%	758734	< 0.001	0.914
LCSR1 + TRIGRAM2B - NED	> - 0.210	96.5%	95.2%	762494	< 0.001	0.916
TRIGRAM2B - 2xEDR	> - 1.400	95.6%	95.6%	755049	< 0.001	0.912
LCSR1+TRIGRAM2B - 2xEDR	> - 1.030	95.4%	95.4%	747771	< 0.001	0.907
EDR + NED - TRIGRAM2B	< 1.300	95.4%	95.8%	755063	< 0.001	0.912
LCSR1 +TRIGRAM2B - EDR - NED	> - 0.955	96.3%	95.4%	762420	< 0.001	0.916
LCSR1 + TRIGRAM2B - 2xNED	> - 0.870	95.4%	95.6%	751409	< 0.001	0.910
LCSR2 +TRIGRAM2B - 2xEDR	> - 0.960	95.4%	95.4%	747771	< 0.001	0.907

Table 2. Chi-squared Test. Algorithm's final results.

As indicated above, algorithms that use the edit distance (ED) highlight differences between the names being compared. In fact, only one pair (0.2%) from the Control set presented an ED of less than 5, compared with 63.6% of pairs from the Similar set. The median ED was 9 in the Control set versus 4 in the Similar set.

The other algorithms acted in the opposite sense: the greater the similarity between the strings being compared, the higher the value. The former measure how many strings of length coincide in the two names being compared. It was deduced from the data that this information would not be very useful, since a large number of pairs presented a value of zero (34.9% in BIGRAM and 65.5% in TRIGRAM), especially in the case of the Control set, which implied a major deviation to the left of the distribution curve in these two algorithms. However, introduction of the BIGRAM1B and TRIGRAM2B variants highlighted the similarity value of the first or first two letters in the names, respectively. It is important to note this finding, because drugs are stored in alphabetical order in pharmacies, and physical proximity can facilitate error. In fact, it has been observed that 93.8% of pairs from the Control set did not have the same first letter, compared to 17.4% from the Similar Group. Furthermore, only 5 pairs (1.1%) from the Control set had the same first two letters, and of these, 4 belonged to the FP subset. Conversely, 56.2% of pairs from the Similar set had two or more letters in common at the start of the name. Thus, 91.5% of pairs whose first two letters were the same belonged to the Similar set, and 3.8% to the FP subset.

In view of this analysis, it was decided to use TRIGRAM2B to try to improve the result, subtracting it from the algorithms that use the ED. The results confirmed a notable improvement in the behaviour of these complex algorithms.

Lastly, the group that highlighted similarities included algorithms that seek the longest common subsequence (LCS). In this case, 81.5% of the Control set presented an LCS below 4 compared with 85.0% of the Similar set which obtained a LCS value greater than or equal to 4. It was also interesting to note that the behaviour of the FN and FP corroborated their shift to the set to which they did not belong.

It should be noted that in order to develop a system for testing potential confusion arising from new drug names, it would be more important to improve specificity. Therefore, when one name was compared with those of approximately 4,000 approved and marketed drugs identified in this study, each basic point (1‰) implied the appearance of 4 FP, equivalent to approximately 2% of sensitivity, since there were around 240 pairs of drug names that had been reported to cause error among those currently approved and marketed in Spain.

When the mixed algorithms are used with the big sample, using more than 4000 different drug names, for each TP the system identifies a mean of 1,110 FP, so the system seemed to be not adjusted, and should be improved with other approaches as a phonetic system which has already showed to improve the results working together with the orthographic one [29,39]. Beside, other points of view in order to search better results would be used, although it would depend on the use of the system. It is not the same problem to implement a system for the approval of new drug names or a program that alert of possible confusion for instance in the administration of a medicine at home, or alerts included in the computer in community pharmacies offices or hospital pharmacies. Each case would

be different and should be studied one by one. For example looking for different cut off points trying to improve the Sensitivity or the Specificity or studying the consequences of the mistake for deciding if a drug name should be changed or not.

CONCLUSIONS

The results confirm that the algorithms differentiated between the two sets of drug names, indicating that they could serve as a useful tool to identify potential confusion between drug names that could lead to medication errors in Spanish.

In any case, the specificity is not high enough for using this system as an only tool. There must be necessary to implement others approaches introducing a phonetic similar system in Spanish and applying quality systems depending on the user and then depending on the objectives of each project. Also is important to point out that cut off points used by each algorithm were looking for the best V of Cramer, an obviously they could be changed in order to improve the specificity against the sensitivity if necessary.

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