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Original Article

Assessment of the readability, understandability, informational contents conformity and usefulness of medication package inserts to Sudanese patients

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ABSTRACT

The objective of this study was the assessment of the readability, understandability, informational contents' conformity and the ultimate usefulness of medication package inserts to Sudanese patients. Two equal sets of thirty one (n=31) package inserts, for same generic names, of European and developing countries produce, were compared using seven core indicators which were, the texts' language, total words count, area (size) to the nearest cm,2 font size, leading in points, frequency of availability of section headings and the presence or absence of nine defined medications' section headings. Results showed significant differences between the words counts and area size of the two groups of package inserts (P value =0.0000 for both). Majority (67.74%) of studied package inserts, were written in English only with much technical terms. The screening of the nine defined section headings, showed significant differences between five of the nine defined section headings, namely, inactive ingredients, use during pregnancy, over dose and management, use after expiry date and date of last version, (P value<0.05). Package inserts' information contents' disparities, texts language and terminology stand as barriers to their readability, understandability and usefulness to patients. To secure package inserts usefulness, official regulators shall standardize their design, typography and informational contents.

Key words: Disparities, information, generic names, medication, package inserts, patients, usefulness.

INTRODUCTION

Pharmaceuticals represent major players in the management of different diseases or ailments. They bear both harms and benefits. They are, in general, self administered and self disposed of. To use them appropriately, patients should be well informed and involved in the agreement for choosing and handling them. That necessitates patient empowerment with sufficient, reliable, accurate, balanced, unbiased, easily accessible, and understandable medication information [1, 2] Physicians and pharmacist rarely provide patients with that sufficiently needed quality medication information.[3, 4] Medication information is usually, provided to patients in verbal, written and/ or visual forms. The amount of verbal information provided to patients by healthcare providers, is criticized for being incomprehensive, deficient, imbalanced, inconsistent, leaving the knowledge and authority in the hands of the caregiver and is easily forgotten. [5, 6] To enhance the recall and understanding of medication information, the verbal information or message should be supported, complemented and reinforced with written and/or visual material.[7] Patients themselves prefer a combination of verbal and written medicines information.[8] The importance and benefits of providing patients with written information about their medications is well documented in the literature.[9,10, 2] In developing countries, where there is a scarcity of independent sources of medication information, PIs are probably the most available source and easily accessible form of

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written medications' information, for both health care providers and patients. [11,12]

The PI had, however, received a lot of criticism to its legibility, readability, understandability, informational contents conformity, comprehensiveness, that might compromise the its resultant usefulness to patients. [13,14] The Sudanese Federal Ministry of Health, through the National Medicines and Poisons Board (NMPB), the official regulator of the registration of pharmaceutical products, is including the package inserts among the various and numerous requirements for the registration of newly submitted pharmaceutical products or formulations files. It, defined the standard format and broad section headings for the design and informational contents of the package inserts [15]. However, it did not define the informational content particulars, overall design of the package inserts, main readability determinants such as the text font size, leading, word count(density), language and style (native language free of technical terms or jargon) which generally and greatly affect the understandability and comprehension of the written medication information. These clear shortcomings were expected to lead to readability, understandability difficulties and disparities in the informational contents particulars of the package inserts of different brands of genetically identical products, belonging to different manufactures. This is even more magnified by the rampant over-the-counter practice and substitution, both legal and illegal, by community pharmacists. These shortcomings may compromise the ultimately targeted usefulness of the package inserts, as they might not provide satisfactory medication information to patients or confuse them to the detriment of their adherence to their prescriptions and /or over-the- counter medications. [16]

To get an initial sensing for the proposed information disparities and other variables limiting PIs usefulness such as readability, understandability, language and technical terms, a small piloting of twenty (n=20) randomly selected package inserts of fourteen (14) generic names representing twenty (20) branded generic products, was conducted. The results of that pilot study confirmed the strength and validity of the abovementioned proposal. Moreover, they were in agreement with similar findings of many studies done in many other developing countries like Saudi Arabia, India, and Palestine [17,19]. It is quite pertaining to know that generics and branded generics from developing countries pharmaceutical producers, represented over 70% of the registered and freely marketed medication products in Sudan[20]. Based on all the above it was decided to conduct this study to assess the readability, understandability, informational contents' conformity which might compromise the usefulness of medication package inserts, to Sudanese patients.

MATERIALS AND METHOD

Sixty two (62) package inserts (PIs), for thirty one identical pairs of same generic names pharmaceutical products, each represented by two different products for two different manufacturers from Europe (innovators, group A, and from developing countries, group B) were carefully and purposefully selected and matched against each other to assess their:-

Readability variables and consequently their ensuing understandability, comprehensiveness; and the consistency (conformity) of their informational contents particulars. The thirty-one generic names selected were found to be available in 18.9 % of the total 3702 registered pharmaceutical preparations in Sudan. Two different package inserts for the same purposefully selected generic name, but of different brands, were randomly selected for the study. They were put in two equal groups, A and B, provided that one of them, the (innovator's product) had to be of a European manufacturer (group A), innovators products serving as a control, while the second (group B) which was considered as the test should be for a product manufactured in one of the developing countries, including Sudan. The selected thirty-one generic names, were found to be available in (n=824) registered pharmaceutical formulations which represented 22.26% of the total registered pharmaceutical formulations in Sudan, (3702). The criteria (core indicators) used in the macro- evaluation of the sixty two selected PIs were:- The language(s) in which they were written mainly English and or Arabic, the size (area) of the package insert to the nearest cm^2**,** which was measured by eye using a millimeter ruler to the nearest square centimeter, the total word count (either Arabic or English), which was indicative of information load or density, the text font size, in points, was defined using ordinary computer built-in facilities, the leadings, vertical spaces between lines of text, defined in points, where one point was equal to the space between two words in a line of the text, the presence or absence of defined main section headings in the PI, the presence or absence of specifically defined nine informational statements (as section headings) in the PI, thought to be complementary to those usually, rarely, included in classical PIs. The language(s) in which the PI was written, the area (size), the total word count of the whole subject package insert (words written in English only or Arabic only); font size

and leading were recorded for all the studied package inserts. The combined total word count, font size, leading for the PIs of those products of the (test group B) of developing countries produce, were compared to exactly same parameters of their generic counterparts of studied PIs for the control pharmaceutical products, from European producers (innovators, group A).

The scoring method for the presence or absence of section headings in the package inserts**,** and the availability or absence of the eleven section headings required by the registration authorities in Sudan in article 14, under the title of the general information about the pharmaceutical product on package inserts were looked for. When the looked-for section heading was present (mentioned), then a score of one (n=1) was given, if not present then the score will be a zero (n=0). The maximum score for section headings was eleven (n=11). The percentage was then calculated. Presence or absences of information in the nine selected information statements (section headings) in the PIs were looked for. The scoring method was the same as the one used for section headings above. The maximum scores were (9x31) 279 for the 31 PIs. Those nine (n=9) general informational statements (specific section headings) looked for in the each of the subject package inserts text were:-
Inactive ingredients (Excipients), therapeutic class, clinical Pharmacology, use during pregnancy and lactation overdose and its management, missed dose and action to be taken, duration of therapy, instructions not to use medications after their expiration dates and date of last revision of information in package inserts. The presence of information won a score of one (1) and the absence won a score of zero (0). The total scores for the PIs of those products from developing countries (test group B) were calculated as a percentage of the maximal score which was 279 (31x 9) and compared to the total scores of those package inserts for products of European (innovators) produce (control group A) which were also calculated as a percentage of the maximal scores. The data were computed and analyzed using the Statistical Package for Social Sciences (SPSS) version 13. Mean Scores and mean word counts were calculated for each of the two groups, separately. Results were then interpreted accordingly. Some of the criteria used in the purposeful selection of the (n=31) generic names medicines for which the PIs were studied were that the selected product: - Had to be registered and freely circulating in both the public and private sectors of the market of pharmaceuticals in Sudan. The product must be in solid dosage form except for Artemether injection, Salbutamol inhaler, Betamethazone topical, Timolol eye drops and Methylprednisolone depot injections, each of which represented a different route of administration.

The following generic names for the purposely-selected products were based on the following general considerations and criteria:--

- Drugs most commonly used in Sudan:- Paracetamol, Diclofenac Sodium, Amoxicillin, Glibenclamide, Chlorpheneramine, Acetylsalisylic Acid and Metronidazole.[21]
- Drug used for long standing ailments (antihypertensive, antiepileptic and antipsychotics):-
  the Antihypertensive selected were: -- Lisinopril, Atenolol and Amlodipine, as representatives of ACE inhibitors, B-blockers and Calcium Antagonists, respectively.
  antiepileptic:- Carbamazepine.
  antipsychotics:- Risperidone
- Drugs commonly used for the most common Sudan endemic diseases:- Malaria, worm infestations: - Artemether injection, Artesunate, Mebendazole.
- Drugs used by patients through devices :-
- Asthma inhaler: Salbutamol inhaler
- *Drugs with narrow therapeutic indices:-* Wararin.
- Drugs most commonly used for peptic ulcers: - Omeprazole (proton pump inhibitors)
- Drugs that interact with most common Sudanese food constituents (Acidic food/juices and soda, soft drinks and dairy products):- Ketoconozole Ciprofloxacin.
- Most commonly used combination drugs:-.
- Cotrimoxazol, Chlordiazepoxide + clidinium bromide.
- Drugs that may cause dependence, on long term use:- Bromazepam.
- Topical corticosteroids representatives:- Betamethazone cream or ointment.
- Depot injectable corticosteroids:- Methylprednisolone.
- Ophthalmic preparations most used for glaucoma:- Timolol eye drops.
- Drugs requiring special dose scheduling and titration:- Corticosteroids, represented by systemic Prednisolone.
- Drugs that have gender specific indications:- Combined Oral contraceptive pills, Doxazocin for benign prostatic hyperplasia (BPH) and Sildenafil tablets for erectile dysfunction.

RESULTS

Comparative evaluation of the characteristics of the (n=62) PIs of groups A and B comprising same medications' generic names.

The following data, as shown in
Table 1, represent the results of the comparative study of the seven core indicators between the European products PIs (n = 31) group A, and their exactly same generic equivalents for PIs of products from developing counties (n = 31), group B,
Table 2, shows the descriptive statistics for the availability of medication information section headings in the sixty-two package inserts and **Table 3,** shows the results of the screening for the medication information in the nine defined informational statements (section headings) in the thirty one pairs of PIs of group A, and group B.
The core indicators used were the language(s) in which the PIs were written, the word count, area of package insert in cm², the font size in points, the leading (vertical space between lines of text) in points, the presence or absence in the PI text of eleven main section headings (comparison) and the presence or absence of nine specified information statement (section headings) of the PIs.

All the studied PIs were for products which were registered and freely circulating in the Sudan market of pharmaceuticals, in both the public and private sectors. Thirty one of them were produced in European countries (group A) and their same generic or branded generic equivalents (n=31) were from developing countries produce. The results of the general comparative evaluation of the characteristics of all the sixty two (n= 62) studied package inserts showed that forty two (67.7%) of them were written in English only while twenty (32.3%) were written in both Arabic and English languages. None of them were written in Arabic (Sudanese native language) alone. Country wise, the thirty one PIs of group (A), the innovators products, were from the following European countries: Germany 7, UK 7, Switzerland 6, France 4, Belgium 4, and only one was from each of Greece, Ireland, and Spain. The thirty-one products of group (B), from developing countries origin, were from, Sudan 12, Jordan 6, Egypt 5, India 3, Syria 2, and one product from each of China, Lebanon, and Pakistan. The comparison of the word count text font size, leading (vertical space between lines of text) and area (size) of the PIs. to the nearest cm² and language provided useful information to the study. The test for significance (2 – tailed) showed that the differences between the word counts and areas (sizes) of the two groups (A and B) were significant (P. value = 0.000).

DISCUSSION

The study results of the languages in which the studied PIs were written, revealed that forty-two (67.75%) selected PIs were written in English only while 20 (32.25 %) were written in both Arabic and English. That was an expected result, as The Sudanese Pharmacy and Poison Act, allowed that the PIs be written in English and/ or Arabic. [15]

This would imply that the patients, who were reported to prefer their own native language; [22] were not the primarily targeted audience for the Sudanese PIs regulators. Other researchers; [23] reported that the provision of oral and written medication information in the patients' own native language, had been linked to improvement in the health outcomes. The Saudi Arabian respondents in one study recommended that the PIs be written in simple Arabic (the native language). [24]

Table 1, shows the result of area (size) of the PI in cm², which when considered together with the total word count of the PI text, though might not inform of the quality and particulars of the written medication information, however they might inform of the quantity of that information, proportionately. Bi-variant analysis using Chi-Square Tests revealed significant differences between both the word count and area (size) of the two compared groups. Other researchers arrived at similar results. [18, 19]

The difference between the areas (sizes), and between the word counts, of the two groups (A and B) were significant, (P. value = 0.000 for both). This shows that the PIs of group A, contain more medication information than those of group B. Again, this was an expected result, as developed countries regulators are keen and have defined advanced rules for patients' and prescribers medication information standards.

The text font size and leading (vertical space between lines of text), of the two group (A and B) which were usually closely linked, as parameters, to the legibility, readability and understandability that might affect the ultimately targeted usefulness of the PIs texts, showed just small insignificant differences, **Table 1.** However, despite that apparent consistency, both the font size and leading were not up to the recommended font size of 11-12 and leading of 1.5.[25 – 27]

The screening of the PIs of the products of the two groups (A and B), for the presence of the main section headings (n = 11), **Table 2**, also revealed some disparities in the presence of the main section headings in the two groups. The presence of the section headings in group (A) won 305 scores (89.44 %) while those of group (B) won 271 scores (79.47 % out of a total of 341scores (100 %). Four

sections headings namely, the main therapeutic class, over dose (signs, symptoms) and treatment, pharmacology, and use in pregnancy and special groups of patients, recorded a combined least presence in the two groups, 25,39,45 and 48 respectively out of a combined total of (62) scores for each section heading. However, the overall availability of main section headings in the two groups of PIs, were within the acceptable limits of 89.44% and 79.47% for group A and B, respectively. That might be because the manufacturers were keen to satisfy the registration requirements set by Sudanese regulators,[15] and accordingly secure the registration (marketing authorization) for their products.

Table 3, Shows clear differences (disparities) in the medications information between the two groups (A and B), as regards the presence or absence of specially defined nine informational statements (section headings). Section heading for the inactive ingredients, use during pregnancy and other special patients' groups, overdose and its management, use of medication after its expiration and date of last version of PI, showed significant differences (P values = 0.000,0.000, 0.001,0.000, and 0.000 respectively). Many researchers arrived at similar results.[19,28,29] These recorded disparities (non-conformities) in the informational contents between the PIs of those generically identical products, of the two groups, may not only fall short of providing patients with the need level of useful medication information, but may even shake the trust of, and confuse patients who quite often may receive a prescription refills for the same generic name, but with another product (branded, branded generics and generics)that is different in shape, color, size, outer-pack, and informational contents than the one he/she got the time before. According to other researchers, [14,18] for a PI, which is an important source of written medication information for patients, to meet its set objectives of usefulness, its contents and design must be consistent, otherwise its usefulness to the targeted audience, may be compromised.

CONCLUSION

Result showed disparities among the studied PIs of same generic products, as regards their texts' language, legibility, readability, understandability and informational contents. PIs for products from developing countries, were less satisfying to the previously set seven core indicators, than those of the innovators. A small independent group of clinical pharmacists, pharmacologists, clinicians, pharmacists and consumers organizations representatives, be formed to decide on standard package insert design, typography, language and basic medication information contents. Regulatory authorities shall mandate that. Package inserts shall primarily be written for the patients (consumers) in their own native language.

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TABLE 1, Groups statistics of the (62) Package Inserts(PIs) of group A and group B, for area in cm.,^{2} font size in points, leading in points and words count.

Products group	N	Mean	Std. Deviation	Comparative Percentages for group A and B.
Area in cm.^{2}				
Innovators' products (A).	31	862.761	579.28780	72.27%
Developing countries products(B).	31	331.02	192.75989	27.73%
Font size in points				
Innovators' products (A)	31	6.555	1.1884	51.8%
Developing countries products(B)	31	6.097	1.3255	48.29%
Leading (Space between two lines of text) **in points.**			.	
Innovators' products(A).	31	1.032	1249	49.61%
Developing countries products (B).	31	1.048	1503	50.39%
Word Count.				
Innovators' products(A).	31	2327.06	1395.885	76.56%
Developing countries products (B).	31	712.32	566.513	23.44%

There were clear differences between the two group of screened package inserts as regards the area in cm.^{2} and the words counts.

TABLE 2, Descriptive statistics for the availability of medication information section headings in the (62) Package Inserts.

Main section headings advised by the Sudanese regulatory authorities.	**European products(innovators'), group A (n=31)**	**Developing countries products (branded generics) ,group B (n=31)**
Generic name	31	31
Drugs forms (pharmaceutical formulations) available	31	31
Number of doses / pack	29	27
Route(s) of administration	31	30
Pharmacology	23	22
Main therapeutic class	11	14
Indications and doses regimen	31	30
Contraindications, warnings, precautions and drug – Interactions	31	29
Use in pregnancy and special groups of patients	29	19
Side effects	31	26
Over dose, signs, symptoms and treatment	27	12
Total of section headings availability scores	305	271
Percentage availability of section headings.	89.44 %	79.47%

Availability of main section headings in the package inserts of the two groups A and B, showed very small and insignificant differences.

TABLE 3, shows the results of the screening for medications' information in the defined nine statements (section headings), in the thirty one pairs of PIs of the two groups (A and B).

Presence of information statements in PIs.	**PIs for products from Europe group A**	**PIs for products from developing countries group B**	**Sig. test**
Inactive ingredient(s)	21	0	Yes (p value =0.000)
Therapeutic class	15	17	No
Clinical pharmacology	23	21	No
Use during pregnancy	29	17	Yes (p value =0.000)
Over dose and its management	24	11	Yes (p value =0.001)
Missed doses and management	4	2	No
Duration of treatment	10	9	No
Do not use after expiration	13	1	Yes (p value =0.000)
Date of last version of PIs.	24	3	Yes (p value =0.000)
Total scores for the presence of statements each group of PIs (n=31)	163	81	
Percentage of presence out of supposed total	58.42 %	29.03 %	
Mean scores	18.11	9.00	

Differences between the presence of five out of nine section headings namely the inactive ingredients, use during pregnancy and special patients groups, over dose and its management, warning not to use medication after its expiration date, and date of last version of package insert were significant (P = 0.000,0.000, 0.001, 0.0000,and 0.000 respectively).

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