ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Evaluation of drug promotional literatures on angiotensin receptor blockers using World Health Organization criteria

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Submission: 04-06-2022 Revision: 02-10-2022 Publication: 01-11-2022

ABSTRACT

Background: Drug promotional literatures (DPLs) are one of the well-known promotional activities of pharmaceutical industries which are sometimes inaccurate as well as of poor educational value. Angiotensin receptor blockers (ARBs) are one of the most commonly used antihypertensives. Therefore, this study was done to estimate the accuracy of DPLs on ARBs as per the World Health Organization (WHO) criteria. **Aims and Objectives:** The aims of this study were to estimate the accuracy of DPLs on ARBs as per the WHO and to estimate the DPLs for types of claims and appropriateness of claims. **Materials and Methods:** A cross-sectional observational study was carried out for 1 month. All the required information of selected DPLs on ARBs were recorded in a pro forma and were evaluated according to the WHO criteria. **Results:** In this study, a total of 20 (twenty) DPLs were evaluated only on ARBs. It was observed that none of the DPLs fulfilled all the WHO criteria. In this study, some DPLs made multiple claims, as much as five per DPL. Claims were, further, analyzed and divided into appropriate and inappropriate. We have observed that 65.96% claims were appropriate and 34.04% claims were inappropriate. **Conclusion:** This type of study can contribute to make prescribing practices rational as promotional activities influence the prescribing behavior of the health-care provider.

Key words: Angiotensin receptor blockers; Appropriateness; Claims; Drug promotional literature

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v13i11.45523

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

According to the World Health Organization (WHO) medicinal drug promotion refers to "all informational and persuasive activities by manufacturers and distributors, the effect of which is to induce the prescription, supply, purchase, and/or use of medicinal drugs."[1] To convince physicians to prescribe, the manufacturer's product is the main goal of pharmaceutical advertisements. Physicians who are contacted by medical representatives' present sample drugs, token gifts, reminder articles, etc. One of the well-known promotional activities of pharmaceutical industries is to produce advertising brochures which, at times, are inaccurate and of poor educational value.[2] India is now among top five pharmaceutical emerging markets and it is currently valued US 41billion dollar.[3] In India, promotional activities standards are set by self-regulatory code of pharmaceutical marketing practices, January (2007), Organization of Pharmaceutical Producers of India (OPPI 2012), and by National legislation.[4] Attempts have been made to implement these guidelines for a long time. The WHO has published ethical criteria for medicinal drug promotion to support and improve health care by promoting rational use of medicines. It is necessary to critically and scientifically evaluate the promotional material of the drugs as such promotional activities influence the prescribing behavior of the practitioners.[5] It is also found that information through drug advertisements is inconsistent with the code of ethics. Antihypertensive drugs constitute major part among all classes of drugs and out of

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this, angiotensin receptor blockers (ARBs) are one of the most commonly used antihypertensives. Moreover, ARBs have all the metabolic and prognostic advantages over ACE inhibitors. Inadequate and inaccurate information of this group of drugs in drug promotional literatures (DPLs) may give negative impact on rational drug use.

Aims and Objectives

This study was designed with an aim of evaluating the DPLs on ARBs available in Indian market using WHO criteria[1] since it is the backbone of self-regulatory code of OPPI with the following objectives:

Primary: To estimate the accuracy of DPLs on ARBs as per the WHO criteria.

Secondary: To estimate the DPLs for types of claims and appropriateness of claims.

MATERIALS AND METHODS

Study design

This study was cross-sectional observational study.

Study setting

This study was Department of Pharmacology, Tripura Medical College and Dr B.R.A.M Teaching Hospital (TMC), Agartala, Tripura, India.

Study period

This study was one month duration from November 1, 2021, to November 30, 2021.

Inclusion criteria

DPLs on ARBs were included in the study.

Exclusion criteria

DPLs containing fixed dose combinations, reminder advertisements, and drug name lists of ARBs were excluded from the study.

Variables

All DPLs will be evaluated by WHO criteria[1] for the following variables:

1. The name(s) of the active ingredient(s) using either international non- proprietary names or the approved generic name of the drug
2. The brand names
3. Content of active ingredient(s) per dosage form or regimen
4. Name of other ingredients known to cause problems
5. Approved therapeutic uses
6. Dosage form or regimen
7. Side-effects and major adverse drug reactions
8. Precautions, contra-indications, and warnings
9. Major interactions
10. Name and address of manufacturer or distributor
11. References.

Study procedure

DPLs on ARBs were collected from medicine outpatient departments (OPDs) and were selected as per inclusion and exclusion criteria. Required information of selected DPLs were recorded in a pro forma and were evaluated according to the WHO criteria for the above-mentioned variables. Each of the above-mentioned variables was divided into three categories as follows:

- Category 1: Having complete information of the variables,
- Category 2: Having incomplete information of the variables and
- Category 3: Having no information of the variables.

Standard pharmacology text books were used to gather information on above variables so that they can be categorized as category 1, 2, or 3.

In addition to this, claims made in DPLs were also evaluated. While evaluating claims, number of claims was estimated as 0, 1, 2, 3, and ≥4. Types of claims were categorized as follows:

Claims on efficacy

Claims stating about improved effectiveness of promoted drug in terms of disease outcome or a patient outcome solely or in comparison with other group of drugs (e.g., antihypertensive action of arbs and calcium channel blockers) or another brand of the same drug (e.g., tazloc or telma for telmisartan) were considered as claims on efficacy.

Claims on safety

Claims using the word "safe" in the promotional literature or mentioning the word "lesser" or "fewer" in relation to adverse drug reaction and/or drug interaction and/or contraindication were considered as claims on safety.

Claims on cost

Claims pointing out low price of promoted drug in absolute or relative terms or any description related to its better cost effectiveness were taken as claims on cost.

Claims on pharmacokinetic property

Claims describing properties of the drug related to its absorption, distribution, metabolism, half-life, and excretion were considered as claims on pharmacokinetic property.

Miscellaneous claims

Appropriateness of claims on efficacy, safety, cost, and pharmacokinetic property was evaluated either

as appropriate or inappropriate using 13th edition of Goodman and Gilman's the pharmacological basis of therapeutics, 20th edition of Harrison's principles of internal medicine, jnc8 guidelines for hypertension, NYHA guidelines for heart failure, articles published in journals and latest edition of CIMS and MIMS.

Sampling procedure and sample size

All DPLs in relation to ARBs were collected as per convenience sampling during the study period from medicine OPD of the institute.

Analysis plan

Data were entered in EpiInfo statistical software and were presented as frequency and percentage.

Ethical approval

Ethical approval was taken from the Institutional Ethics Committee (Ref no: IEC/SFTMC/2020/3/003).

RESULTS

Analysis of DPLs using WHO criteria

A total of 20 DPLs on ARBs were collected out of which 9 DPLs were on telmisartan, seven on olmesartan, two on losartan, and one each on valsartan and azilsartan. Total 11 (eleven) WHO criteria as depicted in Table 1 were used to analyze DPLs. None of the DPLs fulfilled all the WHO criteria. No DPL provided the name of other ingredients known to cause problems. All the DPLs were incomplete to provide approved therapeutic uses. Only 45% DPLs provided dosage regimens, side effects, Precautions, contra-indications, and warnings. However, all the DPLs mentioned about generic name, brand name, and content of active ingredient per dosage form.

Analysis of claims of DPLs

The DPLs were categorized into four groups based on the number of claims (Table 2). Among the total number of DPLs evaluated, 25% DPLs made only one claim, 35% made two claims, 25% made three claims, and 15% DPLs made four claims or more.

Now, the types of claims made on the DPLs were analyzed (Table 3). A total of 47 claims were made in DPLs. Claims about efficacy were made in 89.36% DPLs, followed by that of pharmacokinetic properties in 8.51% and of safety in 2.13%. There was no claim made on cost. The claims were then assessed for their appropriateness. About 73.8% claims on efficacy and 100% claims on safety were found appropriate, whereas only 25% claims on pharmacokinetic properties were found appropriate. Total 34.04% claims were found inappropriate.

The inappropriate claims with their justification are provided in Table 4. There are some claims made in the DPLs (S. No. 1–8 in Table 4) which were supported by references. However, by thorough evaluation of the given references, it was observed that the claims do not match with the original findings of the research articles. These claims are considered inappropriate and the causes of inappropriateness are displayed in Table 4. One claim (S. No. 9 in Table 4) was found inappropriate as per the description of the standard text book. Four claims (S. No. 10–13 in Table 4) made in DPLs which are not supported by any reference and also not found in standard textbooks and guidelines mentioned in the study tools.

DISCUSSION

DPL is considered as an important source of information about new drugs coming in the market. Clinicians often have to rely on the DPLs provided by the pharmaceutical companies to gather information about drugs. It is suggested that the commercial sources of drug information should be complete with respect to all information related to the drug, because it has a significant impact on the prescribing behaviour.[15] Hence, pharmaceutical companies

Table 1: Completeness of DPLs as per the WHO criteria

Criteria	Number of DPLs (%)		
	Complete	Incomplete	No information
The name (s) of the active ingredient (s) using generic name	20 (100)	0 (0)	0 (0)
The brand name	20 (100)	0 (0)	0 (0)
Content of active ingredient (s) per dosage form	20 (100)	0 (0)	0 (0)
Name of other ingredients known to cause problems	0 (0)	0 (0)	20 (100)
Approved therapeutic uses	0 (0)	20 (100)	0 (0)
Dosage regimen	9 (45)	0 (0)	11 (55)
Side-effects and major adverse drug reactions	9 (45)	0 (0)	11 (55)
Precautions, contra-indications, and warnings	9 (45)	0 (0)	11 (55)
Major interactions	4 (20)	0 (0)	16 (80)
Name and address of manufacturer or distributor	9 (45)	6 (30)	5 (25)
References	11 (55)	6 (30)	3 (15)

DPLs: Drug promotional literatures, WHO: World Health Organization

Table 2: Classification of DPLs based on number of claims

Number of claims	Number of DPLs	Percentage
1	5	25
2	7	35
3	5	25
≥4	3	15

DPLs: Drug promotional literatures

Table 3: Estimation of types of claims in the DPLs and their appropriateness

Claims		Appropriateness	
Types	No (%)	Appropriate (%)	Inappropriate (%)
Efficacy	42 (89.36)	31 (73.8)	11 (26.19)
Safety	1 (2.13)	1 (100)	0 (0)
Cost	0 (0)	0 (0)	0 (0)
Pharmacokinetic property	4 (8.51)	1 (25)	3 (75)
Total	47 (100)	33 (65.96)	14 (34.04)

DPLs: Drug promotional literatures

should provide scientific, correct, unbiased DPLs to clinicians.

In this study, we have evaluated a total of 20 DPLs only on ARBs. It was observed that none of the DPLs fulfilled all the WHO criteria. A similar finding was reported in other studies[2,5,16,17]. We have found that all DPLs provided generic name, brand name, and content of active ingredient per dosage form which is comparable with the findings of earlier studies.[2,18,19] None of the DPLs provided information regarding adjuvant which is similar to the finding of other studies.[2,20,21] In comparison with the findings of an earlier study,[2] we have found that more percentage of DPLs had information about dosage regimen, safety, and drug interactions, so this shows that pharmaceutical companies are now trying to follow WHO criteria. None of the DPLs provided complete information regarding approved therapeutic uses. In contrast to our findings, Kakode and Bhandare[22] and Jindal et al.,[20] found

Table 4: Analysis of inappropriate claims in DPLs

S. No.	Inappropriate Claims	Justification for inappropriateness
1.	In COVID-19 patients with preexisting hypertension, ARB/ACEIs had lower death rate and lower IL-6 level than Non ARB/ACEIs group.	Yang et al.,[6] patients on ARBs/ACE inhibitors had a lower death rate than those on non-ARBs/ACE inhibitors medications. The death was 19.0±1.4 out of 43 versus 14.7±10.7 out of 83. The P value was 0.598. The difference failed to reach statistical significance. The fact was not represented with data.
2.	Telmisartan lowers AF recurrence rate as compared to CCBs. In telmisartan treated group, AF recurrence is 12.9% where as in CCBs treated group the recurrence is 44.2%. The difference is statistically significant (<0.01).	Fogari et al.,[7] 49% of patients treated with amlodipine had a recurrence of AF and 12.9% of patients with telmisartan (P<0.01 vs. amlodipine). The data of recurrence of AF in amlodipine treated group is wrongly displayed.
3.	Telmisartan improves insulin sensitivity.	Negro and Hassan[8], (Rosiglitazone 4 mg+Telmisartan 80 mg/day) improved the insulin sensitivity, not telmisartan alone.
4.	Olmesartan significantly reduces SBP and DBP by 34/18 mmHg within 6 months.	Olmesartan was not given alone to the study subjects, it was added to existing antihypertensive therapy treatment for controlling BP.[9]
5.	Olmesartan reduces carotid arterial wall stiffness within 24 weeks.	Patients who were already on statin were included in the study and this might have influenced the finding. The authors of the paper stated that the number of study participants required to demonstrate significant difference is 92 subjects per group. But, Lower number of participants (44, 42 and 47 patients in 20 mg, 40 mg and 80 mg groups respectively) were included in the study.[10]
6.	Olmesartan causes significant reduction in hsCRP by>20%	Olmesartan treatment had reduced serum levels of hsCRP by 15.1% after 6 weeks of therapy. When pravastatin coadministerd after 6 weeks with olmesartan, hsCRP was reduced by 21.1% after 12 weeks of therapy.[11] So, the result highlighted in the DPL is a combined effect of olmesartan and pravastatin and not olmesartan alone.
7.	BP normalization rate of 69.7% is achieved by Olmesartan.	Only patients with stage 1 hypertension (JNC-7 guidelines) were included in the study.[12] So, the findings of the study cannot be generalized.
8.	Azilsartan is the only recommended ARB in salt sensitive hypertension.	Only Azilsartan was used in the study. No comparison with other ARBs was done.[13]
9.	Olmesartan achieves strong reduction in BP compared to other ARBs.	At the recommended dose of 80 mg once a day, azilsartan medoxomil is superior to the maximal doses of valsartan and Olmesartan in lowering blood pressure.[14]
10.	Bioequivalent to innovator brand.	These claims are not supported by any reference and also not found in standard textbooks and guidelines mentioned in the study tools.
11.	Telmisartan empowered with "SOLUSORB TECHNOLOGY" ensures consistent and fast dissolution leading to predictable drug absorption pattern.	
12.	Telmisartan fortified with UPSORB technology shows faster dissolution and optimum bioavailability.	
13.	Telmisartan is more beneficial than olmesartan for controlling BP in early morning	

DPLs: Drug promotional literatures, AF: Atrial fibrillation, CCB: Calcium channel blockers, hsCRP: High-sensitivity C-reactive protein

that DPLs having approved therapeutic indications in 85.6% and 78% cases, respectively.

In this study, some DPLs made multiple claims, as much as five per DPL. DPLs making two claims each were the maximum in number (35%) which is comparable with the findings (31.2%) of Mali et al.,[2] whereas Parli et al.,[23] found that 61.34% of DPLs making only one claim. Most of the claims were made about efficacy which constitutes 89.36% of the total claims followed by that of pharmacokinetic properties in 8.51% and of safety in 2.13%. Mali et al.,[2] observed that claims about efficacy were made in 92% brochures. In other studies[23,24], it was found that 46% and 77.13% claims were pertained to clinical efficacy. In our study, there was no claim on cost which is similar to the findings (0.02%) of Parli et al.[23]

Claims were, further, analyzed and divided into appropriate and inappropriate. We have observed that 65.96% claims were appropriate and 34.04% claims were inappropriate. In another study, Kakode and Bhandare[22] found that 52.8% claims were authentic, while 47.2% were misleading. In our study, we have found that inappropriate claims were made on efficacy in 30.95% and pharmacokinetic properties in 75%.

Limitations of the study

This study had few limitations. It evaluated only 20 brochures as the study included DPLs on only one group (ARBs) of drugs and DPLs on FDCs were excluded from the study. Our study also did not evaluate the authenticity of the pictures. In future, studies can be done to assess the awareness of the physicians about fulfillment of WHO criteria in DPLs by pharmaceutical companies and alerting them about these facts may help to gain accurate and ethical information from promotional literature.

CONCLUSION

This study can contribute to make prescribing practices rational as promotional activities influence the prescribing behavior of the health-care provider. It is of utmost importance for the treating physician to critically evaluate any source of drug information based on the authentic references before accepting them as scientific piece of information. Development of laws and their implementation by drug manufacturers and awareness of physicians can be beneficial measures in the issue.

ACKNOWLEDGMENT

The authors express their sincere gratitude to the Department of General Medicine and authority of Tripura Medical College and Dr. BRAM Teaching Hospital for their constant support in carrying out the study.

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DB- Reviewed the literature, prepared first draft of manuscript; **LD-** Interpreted the results and manuscript preparation; **PB-** Coordination, statistical analysis and interpretation, preparation of manuscript and revision of the manuscript; **MC-** Design of study, Revision of manuscript; and **RG-** Concept and design of the study, Revision of manuscript.

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Source of Support: Nil, **Conflicts of Interest:** None declared.