ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 08 | August - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EVALUATION OF RATIONALITY OF PROMOTIONAL DRUG LITERATURE OF "TOPICAL & ORAL ANTIFUNGALS" USING WORLD HEALTH ORGANIZATION GUIDELINES- AN OBSERVATIONAL, CROSS-SECTIONAL STUDY

Pharmacology

Dr. S. Archana MD Pharmacology
Dr. G. Jayashree* MD Pharmacology. *Corresponding Author

ABSTRACT

Unethical drug promotion is a common problem worldwide. The objectives of this study were to analyse the promotional materials provided by the drug companies as per WHO ethical criteria for medicinal drug promotion. In this cross sectional, observational study ,a total of 43 drug promotional literatures in the form of flyers, leaflets, and brochures concerned with Topical and Oral Antifungals taken as monotherapy or combination therapy were collected which were available in the hospital . The collected promotional materials of different pharmaceutical companies were compared with WHO's Ethical Criteria for Medicinal Drug Promotion.
Majority of DPLs satisfied only half of the WHO criteria for rational drug promotion and most of them did not fulfill all the specified criteria. Incomplete or exaggerated information in DPLs may mislead and result in irrational prescription. Therefore, physicians should critically evaluate DPLs regarding updated scientific evidence required for quality patient care.

KEYWORDS

WHO, Drug Promotional Literatures, Brochures

INTRODUCTION:

When medicines are used rationally, patients receive appropriate treatment, in doses that meet their individual requirements, for an adequate period of time, with the justifiable lowest possible price. Half of the medications used globally are prescribed irrationally and bought inappropriately by patients, which can lead to poor treatment outcomes, adverse drug reactions and wastage of resources. The huge number of products on the market and easy accessibility of commercial drug information through a network of medical representatives make the selection of the right drug and its proper use is an increasingly difficult task. Drug promotion should lay the foundation for proper behavior concerning the promotion of medicinal drugs, consistent with the search for truthfulness and righteousness(1).

There are Committees that are set up to monitor drug promotion. The regional committees are located at Chandigarh, Mumbai, New Delhi and Chennai. The Central Ethics Committee collects information on unethical advertising practices of Pharmaceutical manufacturers and forwards complaints to drug control authority. The Drugs control Authority is empowered to take necessary legal steps on this unethical promotion (Drugs and Magic Remedies Act for objectionable Advertisement, 1954, clause 4). Studies revealed most promotional materials do not fulfill WHO criteria for promotion of pharmaceutical products. When pharmaceutical companies compete to have a better market share and aggressively promote their drug products there is every possibility of the promotion being unethical.

Fungal infections or mycoses constitute up to 20% of patients seeking dermatology consultation. Fungal infection of skin of may be superficial (Dermatophytes(Tinea), Pityriasis versicolor, candidiasis) and deep which includes mycetoma (madura foot) sporotrichosis, chromoblastomycosis and subcutaneous phycomycosis. Fungal infection can be detected by tissue microscopy, culture, serological methods and Polymerase chain reaction(3).

Antifungals are most commonly used in dermatological conditions like Dermatophytosis, Onychomycosis, Candidiasis, Pitriyasis versicolor, Seborrheic dermatitis etc. Topical antifungals like 1% Luliconazole, 2% Eberconazole, 2% Sertaconazole, Clotrimazole, Ketoconazole, Miconazole, Econazole, Terbinafine , whitfields ointment (3%salicyclic acid plus 6%benzoic acid) and Ciclopirox oleamine are used.Oral antifungals like Itraconazole, Griseofulvin, Terbinafine, Fluconazole are also most commonly used in above mentioned fungal diseases(4).

Few studies have observed that information provided in DPLs is varying with the code of ethics. This can affect the drug prescription, utilization, and sometimes can be irrational. Hence, this study was conducted to critically assess the accuracy of the promotional drug literature of antifungals using the WHO guidelines.

APPRAISAL OF THE DRUG PROMOTIONAL LITERATURE(5)

General Assessment:

Promotional material is made attractive and catches our eye due its design, colors and image. It creates mental links between the drug , indication and image that establishes in the prescribers mind bypassing his/her critical appraisal defenses. The physician must look beyond these distractions for complete information about the drug.

Sometimes key issues like ADRs, contraindications and precautions may be entirely omitted or presented in very fine print.

Presentation of the words-size, color, contrast may be misleading.
Eg: Benefits Disadvantages

Here, although the words are the same font size the color and contrast make the word benefits much more noticeable than word disadvantages.

Drug Name Size: Letters of the generic names should be atleast half as large (actual size, not the font size) of the proprietary names. The generic names should have the same prominence as that of proprietary names (in terms of typography, layout, contrast and other printing features)

PICTURES:

The type of pictures (healthy babies, women, patients, doctors, medicinal products, or other treatment unrelated pictures) and relevance of pictures should also be assessed.

Scientific Table And Graphs

Pseudograph graphical presentation without proper axes , labeling legend

An Area Used For Brief Description Of The Information (Abbreviated Prescribing Information)

The abbreviated prescribing information should include an approved indication or indications for use together with the dosage and the method of use, contraindications, precautions and adverse effects.

Claims Made In Promotional Literatures:

Claims made in the promotional brochures were classified into following seven categories.

1. **Efficacy**
Statements about improved effectiveness of promoted drug as a disease outcome or a patient outcome solely or in.

2. **Safety**
Use of the word "safe" in the promotional text or the mention of reduction in adverse drug reaction and/or drug interaction and/or contraindication.

3. **Cost**
Pointing out low price of promoted drug in absolute or relative terms or any description related to its better cost effectiveness.

4. **Convenience**
Statements stating the comfort of patient, e.g., improved dose, low

frequency of dosage, ease of administration, etc. with or without reasons to support the same.

5. **Pharmacokinetic property**
Properties of the drug related to its absorption, metabolism, half-life, etc.

6. **Pharmaceutical property**
New dosage formulations, different manufacturing procedures,storage facilities, etc.

7. **Extravagant emotional claims**
Any claims or statements not related to patient outcome, disease outcome, or drug.

Supporting Scientific Evidence(References)
- References sustaining the claims were categorized as per the source of material, i.e. journals, review article, web sites, books and other including guidelines, seminar, departmental studies, and prescription information.

OBJECTIVE
The objective of this study is to analyze the promotional materials provided by the drug companies as per WHO ethical criteria for medicinal drug promotion.

METHODOLOGY:
Study Design: This is an observational, Cross-sectional study

Study Center: Institute of Dermatology, Rajiv Gandhi Government General Hospital, Chennai

Study Period: January 2021

Sample Size: 43
The confidence level is estimated at 95% with a z value of 1.96 the confidence interval or margin of error is estimated at +/- 15 Assuming p%=46% and q%=54% (critical variable)

$n = p\% \times q\% \times [z/e\%]^2$
$n = 46 \times 54 \times [1.96/15]^2$
n= 42.41 (Rounded up to 43)

Study Duration: 1 month

Inclusion Criteria:
DPLs in the form of flyers, leaflets, and brochures concerned to Topical and Oral Antifungals taken as monotherapy or combination therapy were collected which were available in the hospital

Exclusion Criteria:
Literature promoting medicinal devices and equipment (insulin pump, blood glucometer, and orthopedic prosthesis), ayurvedic medications, drug monographs, reminder advertisements, drugs' name list, and literature promoting more than one drug or more than one fixed drug combination, documents promoting devices and equipment, orthopedic appliances, reminder cards and drug lists were excluded,

Study Procedure:
The study was conducted after obtaining the approval from the Institutional Ethics Committee, Madras Medical College. Drug Promotional materials were collected from the Institute of Dermatology after explaining purpose of the study.

ASSESSMENT:
The Drug promoting materials which are collected are analysed using "WHO criteria for ethical medicinal drug Promotion" guidelines.

The following are the WHO criteria to be followed by pharmaceutical industries for the completeness of DPL:
1.The names of the active ingredients using either international non-proprietary names or the approved generic names of the drug
2. The brand name
3.Pharmacological data: A brief description of the pharmacological effects and the mechanism of action.
4.Clinical information:
(a) Indications: Whenever appropriate, simple diagnostic criteria should be provided.

(b) Dosage regimen and the relevant pharmacokinetic data:
· average and range for adults and children;
· dosing interval;
· average duration of treatment;
· special situations, e.g.: renal, hepatic, cardiac, or nutritional insufficiencies that require either increased or reduced dosage.

(c) Contraindications

(d) Precautions and warnings (reference to pregnancy, lactation, etc.)

(e) Adverse effects (quantify by category, if possible)

(f) Drug interactions (include only if clinically relevant; drugs used for self-medication should be included)

(g) Overdosage:
brief clinical description of symptoms
non-drug treatment and supportive therapy
specific antidotes

5. Pharmaceutical information:
- Dosage form
- Strength of dosage form
- Excipients
- Storage conditions and shelf-life (expiry date)
- Pack sizes
- Description of the product and package
- Legal category (narcotic or other controlled drug, prescription or non-prescription
- Name and address of manufacturer(s) and importer(s).

6.Reference to scientific literature as appropriate advertisements

RESULTS
Table 1 : Oral And Topical Antifungals In Promotional Material

Oral Antifungals	Topical Antifungals
Itraconazole	Luliconazole
Fluconazole	Clotrimazole
Griseofulvin	Eberconazole
Terbinafine	Sertaconazole
	Ketoconazole

Table 1 represents most commonly promoted oral and topical antifungals

Table 2 Analysis Of Drug Promotional Materials According To World Health Organization (n=43)

Fulfillment of the WHO criteria by Drug promotional literature	Mentioned (Number of) Drug promotional literature)	Percentage
The names of the active ingredients using either international non proprietary names or the approved generic name of the drug	40	93.02
The brand name	43	100
Active drug per dosage form	40	93
Other ingredients known to cause problems i.e. adjuvant	0	0
Mechanism of action	18	41.9
Approved Therapeutic uses	36	83.7
Dosage form	35	81.4
Dosage regimen	33	76.7
Side effects and major adverse drug reactions	25	75.6
Precautions and warnings	26	60.5
Contraindications	25	58.1
Major drug interactions	10	23.3
Name of the manufacturer or distributor	40	93
Address of the manufacturer or distributor	32	74.4
Reference to Scientific literature as appropriate	10	23.3

- Table 2 shows analysis of Drug promotional literature materials according to World Health Organization .
- Of the 43 promotional materials analysed, all of them had the brand name written while approved generic names, indication, active ingredient per dosage form and mechanism of action of the drug were written in 93%, 83.7%, 93% and 41.9% of the drug promotional literature materials respectively.
- None of the promotional materials showed inactive ingredients known to cause problems.
- Many of the Drug promotional literature materials included information regarding the type of dosage form (81.4%) and manufacturer/Distributor's name (93%). However, the manufacturer/Distributor's address was written only in 74.4% of the Drug promotional literature materials DPMs.
- Information regarding side effects, precautions, contraindications were written only in 75.6%, 60.5% and 58.1% of the Promotional materials respectively. Potential drug interactions were mentioned occasionally, 23.6% of the DPM.

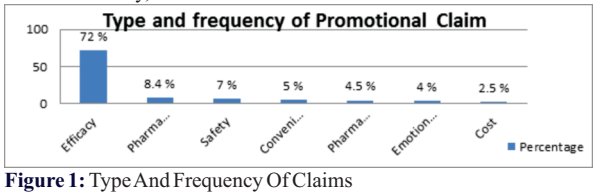

Figure 1: Type And Frequency Of Claims

Figure 1 shows type and frequency of Claims. Of the 43 promotional materials, 54 claims were made.

- Better efficacy of the promoted product than competitors was the dominant claim, 72%.
- Safety, pharmacokinetics and emotional exaggerated claims were made in 7%, 8.4% and 4 % of the Drug promotional literature materials respectively.
- A lower price of the specific products was also claimed in 2% of the Drug promotional literature materials DPMs though none of these did present their current cost.

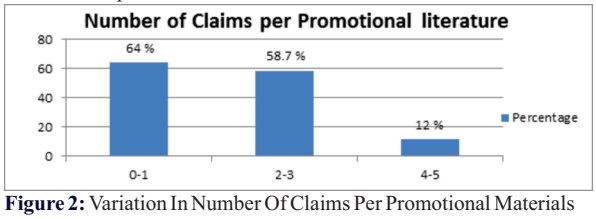

Figure 2: Variation In Number Of Claims Per Promotional Materials

Figure 3 shows variation in number of claims per promotional materials.

64 % of the Drug promotional literature materials had a single claim whereas 58.7 % of them made 2–3 claims per advertisement. This was followed by 12 % of the Drug promotional literature materials which made 4–5 claims.

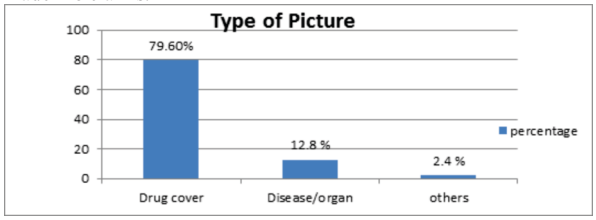

Figure 4: Categorization Of Pictorial Contents Of The Drug Promotional Materials

Figure 4 represents categorization of pictorial contents of the Drug promotional materials

- Pictorial demonstrations were used in 84.4% of the DPMs.

In Majority of the Drug promotional literature materials , 79.6%, displayed the cover of their products followed by pictures of the disease/organ (12.8%) and others like doctor (2.4%)

DISCUSSION

Drug Promotional Literatures are claimed to provide vital drug information and are being utilized to convince health professionals to prescribe the new drug. Many a times, it is the only source on which treating physicians depend on for updating their knowledge about the availability of existing and novel drugs. These are sometimes the only source about the details of new drugs/new indications for old drugs. In our study, it was observed that none of the DPLs fulfilled all the criteria laid down by the WHO guidelines. A similar finding was reported in other studies(6).

An ideal antifungal agent should meet several criteria including the following:
a) To have a broad spectrum of activity against a variety of yeast and filamentous fungi,
b) to be fungicidal rather than fungistatic,
c) to be directed at a specific fungal target and spare interference with host targets including enzymes such as Cytochrome P450, which is responsible for most drug interactions,
d) to have multiple delivery methods, particularly oral availability, to enable prolonged out-patient care, and
e) to have minimal side effects or toxicities. Thus the promotional materials should satisfy the above criteria. (3)

Of the 43 promotional materials analysed, all of them had the brand name written while approved generic names, indication, active ingredient per dosage form and mechanism of action of the drug were written in 93%, 83.7%, 93% and 41.9% of the drug promotional literature materials respectively. This was similar to study done by Vyas al. (7)

In our study, none of the brochures had mentioned other ingredients that are known to cause problems. It was observed that majority of Drug Promotional Literatures quoted dosage form (81.4 %) and therapeutic indications (83.7%), but did not stress on adverse drug reactions, precautions, contraindications, and interactions. The above criteria are certainly necessary for the care of the patient. Similar findings were observed in other studies.(2,6,7)

All the brochures were colorful and attractive, but had irrelevant pictures related to the drugs being promoted which could have been utilized appropriately for listing various properties of drugs, other studies have reported similar finding.(5)

Of the 43 promotional materials, 54 claims were made. Better efficacy of the promoted product than competitors was the dominant claim, 72%. Safety, pharmacokinetics and emotional exaggerated claims were made in 7%, 8.4% and 4 % of the Drug promotional literature materials respectively. A lower price of the specific products was also claimed in 2% of the Drug promotional literature materials DPMs though none of these did present their current cost.

Recent references were mentioned in very few DPLs, but this is essential for updating the clinicians so as to expand their existing knowledge and practice evidence-based medicine. Very few studies regarding evaluation of drug promotional literatures published in scientific medical journals have been reported in India. The study done in Maharashtra found that more than 50% of promoted materials lacking information regarding side effects and precautions.

Another study shows low incidence of completeness of information content in pharmaceutical advertisements indicating a lack of adherence to WHO guidelines. Tandon *et al*. also found that the advertisements in international journals are more complied to the recommendations of the WHO, than Indian journals.

Thus from this study ,it is of utmost importance for the treating physician to critically evaluate any source of drug information based on the established guidelines before accepting them as scientific piece of information. Hence, the treating physicians should learn the art of analyzing DPL to provide quality care for the patients.

CONCLUSION

Drug promotional literature is a major marketing technique in the pharmaceutical industry and busy physicians may at times rely on these promotional literatures. It is a source of information for most busy and practicing physicians. Hence, the information provided in the promotional literature should be factual, evidence based unambiguous and balanced .Unfortunately, most of the times these literatures are neither factual nor evidence based. Treating physicians should be

highly cautious while prescribing the drugs based on information given in Drug promotion materials to avoid irrational prescriptions, higher incidence of drug resistance, adverse effects, and to reduce the cost incurred by patients.

REFERENCES

1. Mali SN, Dudhgaonkar S, Bachewar NP. Evaluation of rationality of promotional drug literature using World Health Organization guidelines. Indian J Pharmacol. 2010 Oct;42(5):267–72.
2. Hailu HG, Gobezie MY, Yesuf TA, Workneh BD. Critical evaluation of the validity of drug promotion materials in Ethiopia. Drug Healthc Patient Saf. 2019;11:47–54.
3. Griffiths CEM, Barker J, Bleiker T, Chalmers RJG, Creamer D, Rook GA, editors. Rook's textbook of dermatology. Volume 4: ... Ninth edition. Chichester, West Sussex Hoboken, NJ: John Wiley & Sons Inc; 2016. 1 p.
4. Tripathi KD. Essentials of medical pharmacology. 2019.
5. Leonardo Alves T, Lexchin J, Mintzes B. Medicines Information and the Regulation of the Promotion of Pharmaceuticals. Sci Eng Ethics. 2019 Aug;25(4):1167–92.
6. Sah P, Sah AK, Jha RK. Evaluation of the rationality of psychotropic drug promotional literatures in Nepal. Journal of Drug Delivery and Therapeutics. 2012 Nov 11;2(6).