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EVALUATION OF PROMOTIONAL DRUG LITERATURE PROVIDED BY MEDICAL REPRESENTATIVE AT A TERTIARY CARE HOSPITAL

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ABSTRACT: Objectives: The study was aimed to evaluate and analyse the drug promotional literature distributed by pharmaceutical companies to physicians. This was done using World Health Organization (WHO) criteria for ethical medicinal drug promotion and International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) Code of Practice, 2012. Detailed analysis of claims was done. **Material and Method**: An observational cross-sectional study was carried out in OPD of a tertiary care hospital. A total of 194 brochures were collected and evaluated according to the WHO criteria and IFPMA Code of practice, 2012. Further claims were categorised and detailed analysis of exaggerated and false claims was done and the authenticity of the brochures was checked. **Results:** None of the brochures gave complete information in accordance to the WHO and IFPMA Code of practice, 2012. Majority of the claims were about efficacy (77.31%) and safety (13.91%). Seven of them were exaggerated and false. **Conclusion**: The study concluded that the drug information provided in the promotional brochures can be incomplete and unreliable with the questionable credibility. Hence a physician should not rely solely on the brochures. They must undergo a strict process of assessment regarding information provided, especially related to efficacy and safety.

INTRODUCTION: "Pharmaceutical product" means all pharmaceutical or biological products (irrespective of patent status and/or whether they are branded or not) which are intended to be used on the prescription of, or under the supervision of, a healthcare professional, and which are intended for use in the diagnosis, treatment or prevention of disease in humans, or to affect the structure or any function of the human body. [1]

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"Promotion" means any activity undertaken, organized or sponsored by a member company which is directed at healthcare professionals to promote the prescription, recommendation, supply, administration or consumption of its pharmaceutical product(s) through all methods of communications, including the internet. One of the well-known promotional activities of pharmaceutical industries is to produce advertising brochures and leaflets. [1]

The literature promoting the drugs and distributed by the drug company representative is an important source of seeking information for the busy medical practitioner. Physician targeted promotion through medical representatives is one of the most common

tactic for drug promotion by pharmaceutical drug companies [2]. Numerous studies have shown that the literature is persuasive in nature rather than educational. [3] It is very important that promotional literature presenting the research findings should provide all information so that the validity of the literature can be ascertained by the physicians. For a better understanding and potential utilization of new drugs on patients, it is very important for a physician to critically analyse research findings and draw conclusions as misleading and wrong information is not uncommon in the literature used for drug promotion. But at times such literatures are inaccurate and of poor educational value. This could also lead to prescribing of more expensive products where cheaper alternatives are available. This may also lead to patient suffering unnecessary adverse effects. These promotional activities create the potential for inappropriate prescribing practices by influencing physicians' prescribing behaviour without necessarily benefiting the patients but contribute to increased health care costs. [4, 5]

Hence the information available to prescriber should be authentic, unbiased and complete in order to enable him to select and use the drug appropriately in a given patient.[6]

Objective: To evaluate and analyse the drug promotional literature distributed by pharmaceutical companies to physicians using World Health Organization (WHO) criteria for ethical medicinal drug promotion [7] and International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Code of Practice, 2012. [1] To categorise and analyse the claims in detail.

Methodology: After taking approval from Institutional Review Board (IRB), an observational cross sectional study was conducted in OPD of tertiary care hospital at Ahmedabad, Gujarat. Promotional drug literature in the form of brochures were collected randomly from OPDs of Medicine, Surgery, Psychiatry, Obstetrics, Gynaecology, Paediatrics, Dermatology, ENT, Endocrinology, Cardiology, Ophthalmology, Nephrology & Urology, Neurology, Oncology and Orthopaedics. A total of 194 brochures were collected within 2 months which was followed by evaluation of the brochures according to the WHO criteria for ethical medicinal promotion.

According to the criteria, following information should be mentioned in a promotional literature:

- INN of active substance
- Brand name
- Content (per dose)
- Name of other ingredients
- Approved use
- Regimen
- Side effects
- Adverse drug reaction
- Contraindications
- Precautions
- Interactions
- Name and address of manufacturer
- References.

According to IFPMA code of practice 2012, all printed promotional materials must include:

- The name of the product (normally the brand name);
- The active ingredients, using approved names where they exist;
- The name and address of the pharmaceutical company or its agent responsible for marketing the product;
- Date of production of the advertisement; and
- "abbreviated prescribing information" which should include an approved indication or indications for use together with the dosage and method of use; and a succinct statement of the contraindications, precautions, and side-effects.

All the brochures were evaluated accordingly and the data was entered in a Microsoft Excel sheet which was then analysed. In addition to this information, promotional materials make various claims about the medicinal products presented in it. Claims made in the promotional brochures were classified into following six categories like:

- Efficacy
- Safety
- Cost
- Convenience
- Pharmacokinetic properties
- Pharmaceutical properties

Moreover, references mentioned in the brochures were authenticated using Martindale: The complete Drug Reference, 37th Edition and www.drug.com website.[8, 9]

RESULT: A total of 194 brochures were evaluated. The authors' self-designed a grading system to grade these brochures.

Grade 1 was allotted to those brochures which had complete information and **Grade 2** was allotted to those brochures where information was incomplete or absent. (**Table 1, Fig. 1**)

TABLE 1: ANALYSIS OF BROCHURES USING WHO CRITERIA

	Complete (Grade 1)	Incomplete (Grade 2)	Percentage (of Complete)
INN of active substance	191	3	98.5
Brand name	194	0	100
Content	153	41	78.9
Name of other ingredient	155	39	79.9
Approved use	173	21	89.2
Regimen	74	120	38.1
Side effect	32	162	16.5
ADR	46	148	23.7
Contraindication	47	147	24.2
Precautions	47	147	24.2
Interactions	34	160	17.5
Name and address of manufacturer	105	89	54.1
References	83	111	42.8

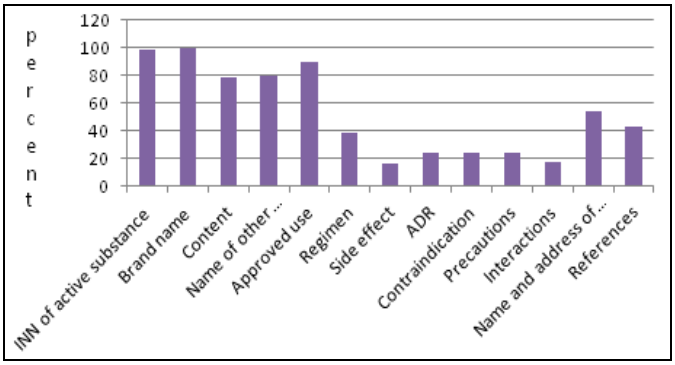

FIG. 1: PERCENTAGE OF PROMOTIONAL DRUG LITERATURE MEETING THE WHO CRITERIA

Based on the analysis of brochures using the WHO criteria, INN of active substance was mentioned in 191 brochures (98.5%). Brand name was mentioned in all the brochures. Content of drug was mentioned in 153 brochures (78.9%). Name of other ingredient was mentioned in 79.9% of brochures. Approved use of a particular drug was mentioned in 173 brochures (89.2%). Drug Regimen was mentioned only in 74 brochures which is just 38.1% of total. Side effects were mentioned only in 32 brochures which accounts for just 16.5 % of the total. Adverse drug reactions were mentioned in 46 brochures that is only 23.7% of the total. Contraindication and Precautions were mentioned in 47 brochures which is only 24.2% of the total brochures. Interactions with other drugs were mentioned in 34 brochures (17.5%) only. Name and address of the manufacturer was mentioned in 105 brochures (54.1%). References were given in 83 of them which is 42.8% of the total.

Based on the analysis of brochures using IFPMA Code of practice 2012, brand name was mentioned in all the brochures. Active ingredient was mentioned in 98.5% of the brochures. Name and address of manufacturer was mentioned in 54.1% of the total brochures. None of the brochures mentioned date of production of advertisement. Abbreviated prescribing information was mentioned in less than 30% of the brochures.

Claims: One more thing was found in promotional drug literature was presence of claims related to the drug. The claims were analysed using standard Reference books and Textbooks of pharmacology. **(Table 2)**

Among the total number of brochures evaluated, 119 (61.34%) brochures made a single claims. 36 (18.55%) brochures had more than one claim and 39 of them (20.10%) failed to mention any claim. Then claims were categorised into 6 categories (**Table 3).**

Most of the claims were made about efficacy and safety which constitute of 91.23% of the total brochures. Very few of them claimed about cost, convenience, pharmacokinetics & pharmaceutical properties. Also, detailed analysis of claims was done (**Table 4).**

TABLE 2: CLASSIFICATION OF BROCHURES BASED ON NO. OF CLAIMS

No. of claims	No. of brochures	Percentage
0	39	20.10
1	119	61.34
2	27	13.91
3	7	3.60
4	2	1.03

TABLE 3: CLASSIFICATION OF BROCHURES BASED ON THE TYPE OF CLAIMS

Category	No. of brochures (194)	Percentage (%)
Efficacy	150	77.31
Safety	27	13.91
Cost	5	0.02
Convenience	14	0.07
Pharmacokinetic	4	0.02
Pharmaceutical	2	0.01

TABLE 4: DETAILED ANALYSIS OF THE CLAIMS

S. No.	Content	Indications	Claim	Anticlaim
1	Timolol	Chronic open angle glaucoma and ocular hypertension.	India's no. one Timolol	Exaggeration. PG analogues are more effective than Beta blockers and have less systemic side effects and safer in old patients.[10]
2	Ofloxacin + Cefixime	Uncomplicated UTI	The gold standard Ofloxacin	Exaggeration Uncomplicated UTI is managed by single antimicrobial agent (Fluroquinolones) and never a combination of antimicrobials.[20]
3	Clarithromycin	Skin and soft tissue infections Infections due to chlamydia, mycoplasma and K.Pneumoniae.	First line broad spectrum macrolide	Exaggeration Azithromycin and Erythromycin also have the same spectrum and they are the first line macrolides.[21]
4	Tamoxifen	For ovulation induction.	Better than low dose Clomiphene	Exaggeration Tamoxifen can cause endometrial carcinoma and the efficacy is similar to Clomiphene.[22]
5	Chlorthalidone + Atenolol	Stage 2Hypertension.	The most trusted antihypertensive in its class.	Exaggeration There are other antihypertensive combinations with similar efficacy [20]
6	Multivitamin	Improves Memory, Cognitive function, Tinnitus. For healthy vision Boost immunity.	India's first memory enhancing multivitamin and mineral supplement	False Multivitamins have not been documented as memory enhancers [23]
7	Telmisartan + Chlorthalidone	Uncontrolled hypertension.	Reduces TC, LDL-C and TG	False The combination worsens the lipid profile of a patient [24]
8	Montelukast + Fexofenadine	Allergic rhinitis	Cardio safe	False Fexofenadine causes QT interval prolongation and Churg-Strauss Syndrome is caused by Montelukast so, this combination is not cardio safe.[20]

DISCUSSION: Pharmaceutical marketing, sometimes called medico-marketing or pharma marketing in some countries is the business of advertising or otherwise promoting the sale of pharmaceuticals or drugs. Pharmaceutical companies use various ways for promotion like brochures, medical representatives, advertisement, online promotion etc.

In an ideal world, physicians would learn all they need to know about drugs from medical literature, and good drugs would thereby sell themselves but we are a long way from ideal. The amount spent on promotion of drugs approximates or perhaps even exceeds that spent on research and development.[1]

There are many Code of practices [10] developed for ideal drug promotion but the drawback is they are not followed by the pharmaceutical companies and they have been vulnerable to criticism for some of their marketing practices.

The information provided for drug promotion should be accurate, scientific and evidence based to keep the physicians well informed.[11] But it is a known fact that the promotional practices carried out by pharmaceutical industries are persuasive in nature. The commercial sources of drug information should be complete with respect to all information pertaining to the drug because it has a great impact on the prescribing behaviour. [12]

The inaccurate and incomplete information provided by these literatures may mislead clinicians in the selection of drug therapy for their patients. The ultimate goal of medical practice is to ensure the care, cure and safety of the patient. [13]

Development of laws and their implementation by drug manufacturers, practitioners' awareness and strengthening of existing guidelines can be beneficial measures in the issue. [14]

In this study, a total of 194 brochures collected for a tertiary care hospital were evaluated. After evaluation of all the brochures, it was established that none of the brochures contained complete information according to the WHO criteria.

INN of active substance was mentioned in 98.5% of brochures and Brand name was mentioned in all the brochures. In a similar study done by Smita N. Mali et al, evaluated 513 brochures using WHO criteria, INN was mentioned in 95.9% and Brand name in all the brochures. [4] Similarly according to another study done by Yogesh A. Garje et al, INN was mentioned in 98% of brochures and brand name in all the brochures. [15]

Approved indication was mentioned in 90% of the brochures in this study. In a similar study done by Smita N. Mali et al, 86.3% of the brochures mentioned it. [4] Similarly according to another study done by Yogesh A. Garje et al, 97% of the brochures mentioned it. [15] Hence physicians should always consult reliable sources of drug information before prescribing a drug.

Content was mentioned in 78.9% of the brochures in this study and study done by Smita N. Mali et al, it was mentioned in 79.5%.[4] Also according to another study done by Yogesh A. Garje et al, it was 82% of the total.[15]

Regimen was mentioned in 38.1% of the brochures. In the study done by Yogesh A. Garje et al, it was mentioned in 40% of the total brochures.[15]

But the information about safety such as side effect, ADR, contraindication, precaution was mentioned in less than 30% of the brochures in this study. In a similar study done by Smita N. Mali et al, it was mentioned in 8.8% [4] and according to another study done by Yogesh A. Garje et al, 5% of the brochures mentioned it. [15] These findings can also be compared to Russian study where only 5% of the promotional drug literature mentioned the complete safety information.[16] The name and address of the manufacturer and references were mentioned in 54.1% and 42.8% of the brochures respectively. In a study done by Jadav SS et al, they were mentioned in 83.33% and 2.06% respectively. [17]

Claims were also categorized. In our study it was noted that majority of the brochures (61.3%) had atleast one claim. Most of the claims were based on efficacy (77.31%). These claims are basically highlighting the superiority of the pharmaceutical product. This is comparable to a similar study by Gurpreet et al, where claims related to efficacy were found in 70% of the brochures.[18]

Claims related to safety claims were found in 13.91% of the total brochures. These safety claims in an ideal environment should be well supported by reliable, retrievable references.

Pharmaceutical companies are known to highlight the positive aspects of their products while hiding the medical aspects. This can be compared to a similar study by Mali et al where safety claims were mentioned in 37.2% of the brochures.[4]

As far as the detailed analysis of the claims was concerned, they were categorised as exaggerated or false claims. A total of 7 such claims were identified by the authors. The first exaggerated claim dealt with Timolol as the first line drug for chronic open angle glaucoma. This claim had been correct if it was said 10 years back. With the current scenario, this claim is an exaggeration because the PG analogues are more efficacious, cost effective and have less systemic side effects.

The second exaggerated claim emphasise that Ofloxacin and Cefexime combination were gold standard for uncomplicated UTI. Uncomplicated UTI should always be managed by a single anti-microbial agent. It should never be managed by third generation Cephalosporin.

The third exaggerated claim focused on Chlarithromycin being the first line macrolide for skin and soft tissue infections and infection by atypical microorganisms. This is exaggerated because azithromycin and erythromycin also have

the same spectrum. The other exaggerated claim dealt with tamoxifen being better for induction of ovulation in comparison to clomiphene. Tamoxifen may be useful in this condition but it has side effects like hot flashes and endometrial carcinoma which can arise from repeated use.

The last exaggerated claim was based on management of stage 2 hypertension with chlorthalidone + Atenolol as the most trusted antihypertensive combination. This claim was exaggerated because there are other antihypertensive combinations with similar efficacy.

On analysis of false claims, the first one dealt with Multivitamin as memory enhancers. This claim is unsubstantiated. The other false claim which was identified was Telmisartan with Chlorthalidone combination claiming to be reducing the total cholesterol, triglyceride and LDL. This claim is false since the Chlorthalidone component in this combination is known to worsen the lipid profile.

The last false claim was observed claiming Montelukast and Fexofenadine combination to be cardio safe. This is also not true since Fexofenadine can cause QT interval prolongation and rare cardiac syndrome Churg- Strauss is associated with Montelukast. (**Table 4**)

On analysis of these claims, many of them being exaggerated or false, a mechanism has to be generated in our country to monitor the drug promotional campaign by pharmaceutical companies.

In India, such regulations need to be strengthened. On the other side till the improvement s are done physicians who are the prescribers should not rely solely on the promotional brochures. They should go for reliable sources of drug information and follow evidence based information regarding prescribing of drugs.

This study evaluates one type of promotional activity of pharmaceutical company i.e. printed promotional literature, however, interventional research to assess the awareness of the physicians about these facts and alerting them about the same will help gain accurate and ethical information for promotional literature. [19]

Our study had the following strengths, it being the first study at our setup of a tertiary care hospital. The promotional drug brochures were compared to 2 standard guidelines, the WHO criteria and IFPMA Code of practice 2012. Our study also showed detailed analysis of false and exaggerated claims.

This study had few limitations, because of shorter duration and comprise of 194 brochures only, the promotional brochures could not be compared to promotional brochures circulated in the western countries. Our study also did not evaluate the authenticity of the references.

CONCLUSION: The study concluded that the drug information provided in the promotional brochures can be incomplete and unreliable with the questionable credibility. Hence a physician should not rely solely on the brochures. This becomes all the more relevant in case of resident doctors who have less experience with the medicines and take the message of the brochure as an authentic content. All brochures circulated among prescribers must undergo a strict process of assessment regarding information provided, especially related to efficacy and safety. Further advertisements which do not confirm with the standard guidelines should not be allowed to be circulated. This pilot study is successful in highlighting the areas which need improvement as far as promotional brochures are concerned.

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