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Patrícia C Mastroianni[I]

Ana Regina Noto[II]

José Carlos F Galduróz[II]

Psychoactive drug advertising: analysis of scientific information

ABSTRACT

OBJECTIVE: According to the World Health Organization, medicinal drug promotion should be reliable, accurate, truthful, informative, balanced, up-to-date and capable of substantiation. The objective of the present study was to review psychoactive drug advertisements to physicians as for information consistency with the related references and accessibility of the cited references.

METHODS: Data was collected in the city of Araraquara, Southeastern Brazil, in 2005. There were collected and reviewed 152 drug advertisements, a total of 304 references. References were requested directly from pharmaceutical companies' customer services and searched in UNESP (Ibict, Athenas) and BIREME (SciELO, PubMed, free-access indexed journals) library network and CAPES journals. Advertisement statements were checked against references using content analysis.

RESULTS: Of all references cited in the advertisements studied, 66.7% were accessed. Of 639 promotional statements identified, 346 (54%) were analyzed. The analysis showed that 67.7% of promotional statements in the advertisements were consistent with their references, while the remaining was either partially consistent or inconsistent. Of the material analyzed, an average 2.5 (1–28) references was cited per advertisement. In the text body, there were identified 639 pieces of information clearly associated with at least one cited reference (average 3.5 pieces of information per advertisement).

CONCLUSIONS: The study results evidenced difficult access to the references. Messages on efficacy, safety and cost, among others, are not always supported by scientific studies. There is a need for regulation changes and effective monitoring of drug promotional materials.

DESCRIPTORS: Psychotropic Drugs. Drug Promoter. Products Publicity Control. Medication Systems, Hospital. National Drug Policy. Review [Publication Type].

INTRODUCTION

According to the World Health Organization (WHO), medicinal drug promotion should be reliable, accurate, truthful, informative, balanced, up-to-date and capable of substantiation. Text and illustration contents should be consistent with scientific information.[20]

Non-ethical medicinal drug promotion is a major issue worldwide leading to irrational drug use, overprescription, self-medication and drug abuse.[1,10,11] This is a more serious issue in developing countries such as Brazil. Studies have shown that promotional materials in medical journals in Brazil, the UK and the US have different contents,[16] evidencing a double standard. The contents

[I] Departamento de Fármacos e Medicamentos. Faculdade de Ciências Farmacêuticas. Universidade Estadual Paulista Júlio Mesquita. Araraquara, SP, Brasil

[II] Departamento de Psicobiologia. Escola Paulista de Medicina. Universidade Federal de São Paulo. São Paulo, SP, Brasil

Correspondence:
Patrícia C Mastroianni
Faculdade de Ciências Farmacêuticas da UNESP
Rodovia Araraquara-Jaú km 1
14801-902 Araraquara, SP, Brasil
E-mail: pmastro@fcfar.unesp.br

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of Brazilian advertisements are more subjective and incomplete compared to same drug materials advertised in the UK and US.[3,15,16]

Several studies[1,7,12] and systematic reviews[19,24] have described the effect of drug promotional materials on medical prescription. Above all, it is a more serious issue for psychoactive drug advertising since it tends to be less informative than other medicinal drug promotional materials.[4,9] In addition, these advertisements usually reinforce stereotypes of the association between gender and psychiatric conditions, showing a disproportion between women and men.[14,15]

Studies have also reported both misinformation and unbalanced information in drug promotion supporting their use: indication, presentation and dosage are often included and highlighted by larger font sizes and colorful text, whereas information restraining drug use, such as contraindications, warnings, precautions and adverse reactions, when available, are less evident and not as visible.[15,17,22] However, these studies have not investigated the consistency between promotional claims and related cited references.

Few studies[5,23] have addressed reliability, accuracy and truthfulness of information in drug promotional materials and their related cited references. Although it is a major issue and a requirement for complying with international recommendations,[20] national drug regulations (Ministerial Decree No. 3.916/98[a]), and current health law (Collegiate Board of Directors' Resolution [RDC] No. 102/00[b]), there is no study to date addressing it in Brazil.

The purpose of the present study was to review psychoactive drug promotional materials targeted to physicians as for consistency of information with their related references and to assess accessibility of the cited references.

METHODS

The study sample consisted of psychoactive drug advertising materials to physicians provided by pharmaceutical promoters in clinics, hospitals and health units. Data was collected in the city of Araraquara, Southeastern Brazil, in 2005.

Psychoactive drugs are prescription only medicines subject to special control and prescription retention. They can only be advertised to prescribers and dispensers (RDC 102/00[b], Art. 5a; Art. 13 and HSS/MoH Administrative Rule No. 344/98[c] - Art. 12, item II; Art. 16) through promotional materials both delivered at health settings, and published in medical journals and books.

Pharmaceutical companies disseminate the same drug advertising materials nationwide. Thus, materials collected in the city of Araraquara can be deemed representative of psychoactive drug advertisements distributed to prescribers nationwide.

For data collection, physicians in hospitals, clinics and health units were contacted and the purpose of the study was explained. Those who agreed to participate were asked to voluntary retain all promotional materials for the team's monthly collection.

No differences were seen in materials collected by site of collection since the same promoter of each pharmaceutical company used to visit the hospitals, clinics and health units and provide the same materials.

References were requested from physician and pharmaceutical customer services (PPCS) through the number provided in the promotional materials. The references made available by PPCS were sent through mail and searched in UNESP (Ibict, Athenas), and BIREME libraries (Scielo, Pubmed, free-access indexed journals) and other on-line databases available, such as CAPES journals.

Reference information on access source (laboratory, library or unknown) and review status (reviewed, not reviewed and reason for no review) were entered into a database.

Content analysis of each reference obtained followed a guide developed based on a "floating reading" of promotional materials and their related references.[2]

The guide included the following:

- Part I – Promotional material information: ID number, drug name, active component, class of therapeutic agent, pharmaceutical company name, PPCS number; cited references and number of references cited;
- Part II – Review of cited references: type of reference (published and indexed; published and non-indexed; unpublished article; book citation; pharmaceutical material; meeting presentation; association handbook; drug price guide); study category (meta-analysis; clinical trial; cohort study; case-control study; editorial; review; survey; pharmacovigilance study), and consistency level (consistent; inconsistent or somewhat consistent with promotional claims).

[a] Brasil. Portaria n° 3.916, de 30 de outubro de 1998. Aprova a Política Nacional de Medicamentos. Diário Oficial da União. 10 nov 1998.
[b] Brasil. Resolução RDC nº 102, de 30 de novembro de 2000. Aprova o Regulamento sobre propagandas, mensagens publicitárias e promocionais e outras práticas cujo objeto seja a divulgação, promoção ou comercialização de medicamentos de produção nacional ou importados, quaisquer que sejam as formas e meios de sua veiculação, incluindo as transmitidas no decorrer da programação normal das emissoras de rádio e televisão. Diário oficial da União. 1 dez 2000.

To prevent both subjective and differing interpretations, content analysis was conducted in duplicate by independent reviewers. In case of disagreement, a third reviewer would review the content. References were classified according to study category and level of evidence and grade of recommendation.[21]

"Consistent" information was defined when promotional claims were found in the cited reference; "somewhat consistent" information was defined when at least one claim or part of it was found in the cited reference; and "inconsistent" information was defined when promotional claims were not found in the cited reference.

A database was electronically created in a flow chart to manage data collected.

The study was approved by UNIFESP Research Ethics Committee (Protocol No.176/06).

RESULTS

There were collected 167 different psychoactive drug advertising materials from 25 pharmaceutical companies. Most of them promoted antidepressive (41.9%) and anxiolytic drugs (24.5%). Fifteen promotional materials (from four pharmaceutical companies) were excluded as they did not provide any references.

Of 152 promotional materials reviewed, there were on average 2.5 (1–28) references cited per piece, making a total of 395 references. In their body, there were identified 639 pieces of information that were clearly associated to at least one reference cited (mean 3.5 pieces of information per material) (Figure).

Table 1. Reasons for difficult access to cited references in psychoactive drug advertising materials. Araraquara, Southeastern Brazil, 2005.

Reason	N	%
Articles not available or not provided by physician and pharmaceutical customer services	52	39.4
Drug price guides	22	16.7
Posters or presentations in scientific meetings	15	11.4
Books	10	7.6
References not cited in promotional materials	9	6.8
Unpublished pharmaceutical material	7	5.3
Unpublished sales report	5	3.8
Incomplete/inaccurate references	5	3.8
Articles written in French	3	2.3
Articles written in German	3	2.3
Brazilian government official newspaper	1	0.6
Total	132	100

Two pharmaceutical companies refused to provide the requested references. Although most companies claimed they did not have any references in their files, all those who agreed to collaborate said they will ask their headquarters or medical libraries to provide the requested references. It took three days to six months for companies to send them. Only one pharmaceutical company provided all references requested; the remaining provided on average less than 50% of references cited and 107 (27%) references were directly obtained. The remaining 156 (39.5) references were accessed in libraries or other database referred in Methods. A total of 263 were obtained. The remaining references (132; 33.5%) were either not available in the companies' headquarters or were not indexed in the database searched or unpublished (Table 1).

Most references were from studies published in indexed (291; 73.7%) or non-indexed (13; 3.3%) journals. Based on these 304 references, 260 studies were categorized through accessing their abstracts or entire content.

It was found that the majority of studies were clinical trials (N=116), meaning the highest level of evidence for therapeutic choice, followed by literature reviews (N=94), meaning the lowest level of evidence for therapeutic choice.[21] In addition, there were found non-recommended studies such as pre-clinical studies (N=12), epidemiological surveys (N=6) and life quality assessment (N=1) (Table 2).

In regard to the level of consistency between promotional claims and the related cited references, of 263 references available (107 provided by pharmaceutical companies and 156 obtained from libraries and database), 346 claims were reviewed, 54% (346/639) of all claims identified in the advertising materials collected.

Table 2. Study categories of studies referenced in psychoactive drug advertising materials. Araraquara, Southeastern Brazil, 2005.

Study category	N	%
Recommended		
Clinical trial	116	44.6
Meta-analysis	8	3.1
Cohort study	8	3.1
Pharmacovigilance/case study	9	3.5
Reviews/Guides	94	36.1
Editorial	6	2.3
Not recommended		
In vivo/in vitro pre-clinical study	12	4.6
Epidemiological survey	6	2.3
Quality of life assessment	1	0.4
Total	260	100

In most claims reviewed (234; 67.7%), sentences or information were identified in the cited reference. In 15.6% (54), information was either incomplete or partly referred to the reference cited; and in 16.7% (58), no information was found in the reference cited.

Inconsistent or somewhat consistent content was due to missing or conflicting information found in the referenced studies, i.e., different drugs studied, reviews of classes of therapeutic agents that did not provide specific information on the promoted drug, and different population studied, e.g., young adults when it claimed to be "(…) safe for the elderly". There were also found pieces of information including extrapolated results with increased level of statistical significance; animal studies but claims were for humans; studies in patients with a single condition and claims about the drug efficacy for patients with two or more conditions or even about the efficacy in patients with co-morbidities (e.g., renal or liver failure) not investigated in the study (Table 3).

Table 3. Reasons for inconsistency or partial consistency between claims in psychoactive drug advertising materials and related references. Araraquara, Southeastern Brazil, 2005.

Reason*	N	%
Missing information	87	62
Extrapolation regarding indication/ conditions/class of therapeutic agent	12	12
Conflicting information or misinformation	14	10
Extrapolation to humans	8	5.6
Extrapolation of statistical data	7	5
Different population studied	6	4
Extrapolation regarding quality of life	2	1.4
Total	141	100

* Each claim may have more than one reason for inconsistency

DISCUSSION

The present study showed difficult access to the references cited in psychoactive drug advertising materials. Villanueva et al[23] (2003) reported similar findings after studying drug advertisements published in six Spanish newspapers. These authors did not have access to 18% of the cited references since they were monographs or unpublished data.[23]

Prescribers would find even more difficult to have access to referenced information in drug promotional materials.

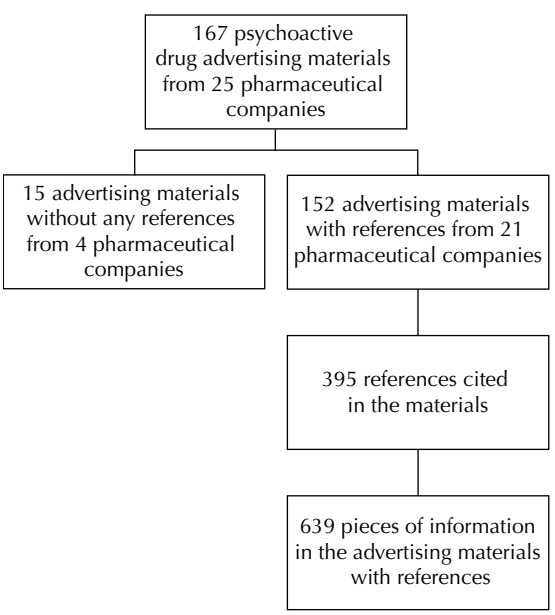

Figure. Flow chart of cited references in psychoactive drug advertising materials reviewed. Araraquara, Southeastern Brazil, 2005.

The present study also evidenced a need for changes in current health laws regarding drug promotion regulations, banning citation of non-scientific based reference, such as drug price guides. Moreover, pharmaceutical companies should be required to make available full original studies in their websites and to cite in promotional material studies designed at the recommended level of evidence for therapeutic choice, preferably published studies rather than posters and presentations given at scientific meetings.

Promotional materials often include incomplete, summarized, inconsistent and different information than that in the referred studies,[8] favorably supporting the therapeutic indication, drug efficacy, safety and cost.[18,19,24] In contrast to previous studies that have reported low citation of references in advertising claims,[15,17,22] in the present study, 91% of the materials reviewed had at least one reference. It can be noted that today pharmaceutical companies tend to provide references as marketing strategies of drug promotion.[23]

Pharmaceutical companies frequently draw on randomized clinical trial studies (44.6%) published in renowned indexed medical journals,[5,23] especially intended for therapeutic choice.[21] On the other hand, 36.1% of references here studied were literature reviews, which are less recommended[21] and in general promotional claims favorably supported drug use and omitted warnings and precautions to specific populations stressed in the reviews. Hence, unbalanced information is usually found in advertising claims.[15,17,23]

A good number of claims reviewed (67.7%) were consistent with the references because consistency was ascertained when the cited information was identified regardless of any other considerations. RDC 102/00, Art. 15, establishes that "citations, tables or other illustrations obtained from scientific publications and included in any advertisements or promotional materi-

als have to be accurately reproduced and cite the full reference". Most citations were from literature reviews that contemplate pros and cons; pros were cited in the promotional materials but only positive results of clinical trials were cited.

Studies have reported publication biases,[6,13] i.e., studies with positive results supporting drug use are promptly published while unfavorable data require much more time to be published or even remain unpublished, which could explain the fact that most claims reviewed were consistent with the cited references. Also, because pharmaceutical companies fund clinical trials, the results are reported as part of their marketing strategies[23] so promotional claims tend to favorably support drug use.[25]

However, it is not known whether the same consistency would have been found if all 132 references not available, accounting for 293 claims that were not reviewed (46%), were accessed.

Inaccurate psychoactive drug advertising was found in 32.3% of information reviewed. A similar finding was reported by Villanueva et al[23] (2003) while studying promotional claims in antihypertensive drug advertisements published in Spanish medical journals and related references (44.1%) and by Gómez-Garcia et al[5] (2005) while reviewing promotional materials provided to primary care physicians in Spain (44.5%).

Ziegler et al[25] (1996) studied the accuracy of drug information provided to physicians by promoters and found that 11% were conflicting. In present study, 10% of inconsistent claims were due to misinformation or conflicting information.

The reasons for inconsistent or somewhat consistent information found in the present study were similar to those reported in other studies in Spain:[5,23] missing information, other drugs studied, patients with conditions not investigated in the studies, statistical differences were not significant, extrapolation of indications and conditions and conclusions other than those claimed in the materials. According to RDC 102/00,[a] it is thus characterized misleading advertising due to information omission or misinformation.

Misinformation was often found in promotional materials claiming efficacy, safety and low costs. Low-cost claims were referenced to drug pride guides. Although cost-effective claims are usually seen in drug promotion,[18] there are required cost-effectiveness analyses comparing treatment costs rather than drug prices.

Health providers have to be more careful and apply their knowledge and better judgment while appraising promotional materials. Pharmaceutical companies are not concerned whether references are correctly cited, references are actually related to the drug promoted and comparisons are made between same classes of therapeutic agents. Health providers are unlikely to judiciously appraise advertising materials provided to them and thus become more prone to be influenced by promotional practices.[19]

In conclusion, the issue requires further discussion. It is proposed content analyses of drug advertising in undergraduate studies, continuing education and permanent education programs to degree providers to encourage rational drug use and to prevent abusive prescription of psychoactive drugs and promotional practices to influence health providers' therapeutic choices.

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[a] Brasil. Resolução RDC nº 102, de 30 de novembro de 2000. Aprova o Regulamento sobre propagandas, mensagens publicitárias e promocionais e outras práticas cujo objeto seja a divulgação, promoção ou comercialização de medicamentos de produção nacional ou importados, quaisquer que sejam as formas e meios de sua veiculação, incluindo as transmitidas no decorrer da programação normal das emissoras de rádio ë televisão. Diário oficial da União. 1 dez 2000.

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