Supported and unsupported claims in medicinal drug advertisements in Indian medical journals

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Abstract

The study assessed 292 supported and unsupported claims in 102 medicinal drug advertisements across 15 Indian medical journals published in 2009. WHO ethical criteria for medicinal drug promotion were applied. None of the advertisements satisfied all the WHO criteria. Safe prescribing information on major adverse drug reactions, contraindications and warnings was provided in only 19 advertisements. Of 292 drug claims, only 80 (27%) were supported with reference(s), of which only 7 (9%) claims were unambiguous, or well substantiated with references. 14 references quoted did not substantiate the claim and 15 constituted weak scientific evidence. Superlatives like "tested", "trusted", "guarantees success" and "matchless safety" were used without evidence to substantiate such claims. Stronger enforcement mechanisms are necessary to ensure reliable drug information in pharmaceutical advertisements.

Introduction

Advertisements are an important means of getting information on medicines to physicians. They are one of the techniques used by pharmaceutical companies to promote their products to physicians (1-3). Information provided in these advertisements should be of high quality to enable physicians to practise evidence-based medicine. However, it has been observed that the information provided in medicinal drug advertisements is often exaggerated, inaccurate and missing critical information on safe prescribing (4). Advertisements which exaggerate the benefits and downplay the risks of a drug, with poorly supported claims, failing to balance claims of efficacy with potential adverse effects, and promoting a drug for groups other than those for whom it is approved, are likely to adversely affect treatment (5-7). Physicians relying on such promotional information may prescribe irrational drugs that endanger their patients' lives (8).

There are three major codes which deal with the promotion of drugs: the International Federation of Pharmaceutical Manufacturers (IFPMA) code of pharmaceutical marketing practices (9); the World Health Organization's ethical criteria for medicinal drug promotion (10); and the code prepared by Health Action International (11). However, despite the availability of regulations worldwide, pharmaceutical advertising in medical journals has been criticised for being of poor quality. The mere existence of specific codes and regulations does not guarantee their enforcement and compliance, as demonstrated by a Brazilian study where 64.3% of prescription drug advertisements found in all sources of drug advertisements in a Brazil city exhibited irregularities (12). Non-compliance with US Food and Drug Administration (US FDA) standards was also observed by Wilkes et al who reported 40% advertisements in US journals as having unbalanced drug information (5).

In India, at present the Magic Remedies (Objectionable Advertisement) Act 1954 deals with misleading promotion (13). The Act prohibits false or misleading advertisements related to drugs. However, there are no guidelines which deal with drug promotion.

Advertisements for promotion of pharmaceuticals are a regular feature of Indian medical journals. They form a major means of communicating drug-related information to the medical community.

The present study evaluated the supported and unsupported claims in 102 medicinal drug advertisements in 15 Indian medical journals.

Materials and methods

All Indian medical journals published in 2009 available in the library of a public teaching hospital were scanned for advertisements. Those journals which did not include any advertisement were excluded from the analysis. From the remaining 15 journals, the latest issue of each journal available in the library rack on the date of the library visit was selected for analysis. (Details of the journals are given in Table 1.) 102 medicinal drug advertisements were assessed. Advertisements referring to medical equipment, surgical appliances and nutritional supplements were excluded.

We assessed each advertisement according to WHO's ethical criteria for medicinal drug promotion to physicians and health-related professionals (10). The criteria include the following:

1. The text should be legible.
2. Advertisements that make a promotional claim should at least contain summary scientific information. (Some countries require an approved scientific data sheet or similar document, for a given period from the date of the first promotion or for the full product life.)
3. The name(s) of the active ingredient(s) using either international non-proprietary names (INN) or the approved generic name of the drug.

Advertisements should also include the following:

4. the brand name;
5. content of active ingredient(s) per dosage form or regimen;
6. name of other ingredients known to cause problems;
7. approved therapeutic uses;
8. dosage form or regimen;
9. side-effects and major adverse drug reactions;
10. precautions, contra-indications and warnings;
11. major interactions;
12. name and address of manufacturer or distributor; and
13. reference to scientific literature as appropriate.

Second, we determined the number of claims made in each advertisement and categorised them into five groups: those pertaining to effectiveness, safety, dosage or convenience and cost, and general or neutral claims. Claims were further classified as "supported" claims if references were supplied, and "unsupported claims" if a reference was not provided.

For all claims supported by references, we obtained original papers or their abstracts for all references available in the public domain and rated them in terms of the quality of evidence as relating to the study design, using a standard "hierarchy of evidence". We conducted internet searches for data held on file by pharmaceutical companies or presented solely at conferences, or in books, reports and newsletters, but were unable to obtain them.

A supported claim was rated as "unsubstantiated" by the cited study if one of the following criteria applied: it was a false statement; it was an exaggeration of efficacy; it selectively concealed information; it misquoted evidence; it exaggerated the drug's safety, or it made an unjustified generalisation. A supported claim was rated as "unambiguous" if the references cited substantiated the claim.

Results

Application of WHO criteria

None of the advertisements satisfied all the ethical criteria set by WHO. The number of advertisements satisfying WHO criteria is depicted in Table 2. Brand name 102 (100%), name of the active ingredient 92 (90%) and approved indications 87 (85%) were commonly mentioned. Safe prescribing information was given less importance. Only 19 of the 102 advertisements provided safe prescribing information such as on side effects, major adverse drug reactions, precautions, contraindications, and warnings. Only 16 gave information on major interactions. A summary of scientific information was provided in 18 of the 102 advertisements. 53 advertisements did not mention any reference to scientific literature.

Supported and unsupported claims

We identified 292 claims from 102 advertisements (Table 3). The claims were categorised into those regarding effectiveness (170), safety (43), dosage or convenience (26), and cost (19), and other, neutral claims (34).

None of the 213 claims related to efficacy or safety was supported by data on absolute risk reduction and number needed to treat.

Of these 292 claims, 212 (73%) were unsupported claims (no references were given).

80 (27%) claims, in 49 advertisements, were supported with a total of 94 references.

These 94 references were two meta-analyses, one systematic review, 38 randomised controlled trials, 19 observational studies and narrative reviews, 3 animal studies and 31 other types of references (reports, newsletters, books, data on file). We were unable to trace references in the last category (31) on the internet or in the library where the journals were located. Therefore, a total of 63 references were examined.

Of 80 supported claims, only 7 (9%) claims were unambiguous claims. These claims were substantiated by 22 references.

Unsubstantiated supported claims

73 (91%) of supported claims were either unsubstantiated or poorly substantiated.

Of the 94 references given, 31 were not available for public searching. Of the 63 references in the public domain, 22 supported the 7 unambigious claims which referred to them. Of the remaining 41 references, 12 could not be traced because they had incorrect or incomplete citation details. (This did not include incomplete or incorrect references which were traceable with considerable effort.) Of the remaining 29, 14 references were false or misleading and did not substantiate the claim made, and 15 references were of a low level of evidence or found to be scientifically weak on examination.

Table 4 contains examples of claims in medicinal drug advertisements which could not be substantiated through the references they cited. 14 of the bibliographical references did not substantiate the claims made. For example, Misoprost-600(r) (Misoprostol 600 mcg) is claimed to be used in pregnancy-induced hypertension. However, the study quoted in support of this claim excluded pregnancy-induced hypertensive patients (14). In another example, an ad for Capiibine(r) (Capecitabine) claimed "improved survival in colorectal cancer compared with 5-FU". However, the study population was of gastric cancer patients and did not claim improvement over 5-FU (15). Preclinical data for a drug was applied to humans. For example, the claim that Infen-25(r) (Dexketoprofen trometamol) was "gentle on GI tract" was supported by an animal study (16).

A total of eight claims cited 15 bibliographical references which appeared to be convincing but were found to be scientifically weak on examination. For example, it was claimed that Yasmin(r) (Drosperinone/ethinylestradiol) ensured "stable body weight" but the reference was an open label trial with an unacceptable drop-out rate of 29% (17). In another example

"predictable bioavailability" claimed for Dytor(r) (Torsemide) was based on an open label, non-blinded trial in patients with heart failure (18).

Some advertisements contained both supported and unsupported claims. Another claim for the same drug stated that it had been "tried, tested and proven in Indian patients," but no reference was provided to substantiate this claim.

Such inconsistencies cast doubt over the validity of such claims.

Discussion

Advertisements are an important source of drug information for physicians and have been shown to influence prescribing patterns (3,8,19,20). Thus, misleading or incomplete information can lead to improper prescribing.

A well-substantiated claim is precise and based on relevant scientific evidence. Research cited in advertisements in medical journals should be evidence-based, meeting basic criteria for validity, significance of results and applicability to the readers' practice.

The majority of drug advertisements in Indian medical journals examined by us (53 out of 102) were unsupported by references to studies to support the claims made. Only 49 advertisements were supported by references. However, 31 of these 94 references were not in the public domain and 12 references were incomplete or inaccurate. Of the remaining, only two were meta-analyses, one was a systematic review and 38 were randomised controlled trials.

Only 7 out of 292 claims were substantiated by appropriate references traceable and accessible in the public domain. Not one of the 213 claims related to efficacy or safety was supported by data on absolute risk reduction and number needed to treat.

Our study found evidence of inappropriate use of references in pharmaceutical advertising in medical journals. A number of references did not support the claim made, and others constituted weak evidence for any claim. This suggests that the fact that references are given is no guarantee that the advertisement claims are valid. Prescription practices based on such claims - for example if promoted for categories of patients who have in fact been excluded from the study - can have adverse consequences for patients.

In a systematic review (21) of 24 studies evaluating the quality of drug advertisements in medical journals, studies of advertisements in developed countries found that the majority of all ads (median 65%, range 51-100%) provided references (except for a study in Spain which found that only 13% of ads provided references). The same review found that in developing countries, 23% of all ads (range 2-59%) provided references. An Australian study found that for 35% of the claims studied, the references were not searchable on Medline (22).

The level of scientific evidence used also assumes great importance. Gutknecht reported that in the US and Canada, references to randomisation and blinding were present in 37% and 47% advertisements respectively (8). In a study of advertisements in Australian medical publications, only 10% claims were supported by level 1 evidence (meta analyses) and 45% by at least one RCT (22).

Inappropriate drug advertisement is as common in India as in other developing countries (23,24). The poor quality of drug advertising is an important issue in India, where independent sources of information on medicines are limited and physicians rely on the drug industry to provide information on drugs.

Conclusion

This study has a number of limitations. The sample size is small and the advertisements were identified through convenience sampling. However, the study findings remain important and suggest the need for active monitoring to keep a check on the quality of pharmaceutical advertisements. Regulators may consider providing explicit requirements on the scientific evidence necessary to support claims in journal advertising. Strong enforcement mechanisms are necessary to ensure that pharmaceutical companies provide reliable information essential for rational prescribing. Physicians on their part should be cautious in accepting advertisement claims even when they are supported by bibliographical references.

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Table 1: Characteristics of journals reviewed

S. No	Journal name	Vol	Issue	Listed in Pubmed	Total pages	% Pages with ads
(1)	*Indian Journal of Anaesthesia*	53	1	Yes	134	7.46
(2)	*Indian Journal of Cancer*	46	3	Yes	92	4.34
(3)	*Indian Journal of Chest Disease and Allied Sciences*	51	3	Yes	72	1.38
(4)	*Indian Journal of Gastroenterology*	28	1	Yes	48	2.08
(5)	*Indian Journal of Opthalmology*	57	4	Yes	140	40.71
(6)	*Indian Journal of Orthopaedics*	43	3	Yes	112	18.75
(7)	*Indian Journal of Paediatrics*	76	5	Yes	130	13.84
(8)	*Indian journal of Plastic Surgery*	42	1	Yes	152	0.66
(9)	*Indian Journal Of Psychiatry*	51	2	Yes	102	7.80
(10)	*Indian Journal of Tuberculosis*	56	2	Yes	64	1.56
(11)	*Indian Journal of Urology*	25	2	Yes	150	10.66
(12)	*Indian Paediatrics*	46	4	Yes	96	6.25
(13)	*Journal of the Indian Medical Association*	107	3	Yes	68	35.29
(14)	*Journal of the Association of Physicians of India*	57	3	Yes	100	14.00
(15)	*The Journal of Obstetrics & Gynecology of India*	59	3	Yes	95	14.73

Table 2: Number of advertisements satisfying WHO criteria for medicinal drug promotion

WHO criteria	Number of advertisements satisfying WHO criteria
Legible text	99 (97.1%)
Summary of scientific information	18 (17.6%)
Approved scientific data sheet	0 (0.0%)
Name of the active ingredient	92 (90.2%)
Brand name	102 (100.0%)
Content of active ingredient per dosage form or regimen	84 (82.4%)
Other ingredients known to cause problems	8 (7.8%)
Approved therapeutic uses	87 (85.3%)
Dosage form or regimen	50 (49.0%)
Side effects and major adverse drug reactions	19 (18.6%)
Precautions, contraindications and warnings	19 (18.6%)
Major interactions	16 (15.7%)
Name & address of manufacturer or distributor	87 (85.3%)
Reference to scientific literature as appropriate	49 (48.0%)

Table 3: Types of promotional claims in medicinal drug advertisements in Indian medical journals

Type of promotional claim	Claim present in number of advertisements N=102	Total number of claims in all advertisements N=292
Effectiveness	72	170
Safety	30	43
Neutral	25	34
Dosage form / convenience	18	26
Cost factors	18	19

Table 4: Examples of unsubstantiated claims in medicinal drug advertisements

S. No	*Pharmaceutical product (active ingredient)*	*Claim*	*Reference*	*Type of reference and reasons for potential bias*	*Type of claim*
(1)	Cipralex(r) (Escitalopram)	"Effectively prevents relapses"	Gorwood P et al. *Am J Geriatr Psychiatry*. 2007 Jul; 15;7. 581-93.	*Single blind RCT* Study population of trial consists of geriatrics (aged ≥ 65 yrs) only	Unjustified generalisation
(2)	Ecosprin(r) (Enteric coated aspirin)	"Optimal efficacy with increased safety"	Petroski D. *Clin Ther* 1993 Mar-Apr;15(2):314-20.	*Single blind RCT* Reference to duodenal mucosal injury omitted	Selective information Concealment
(3)	Glynase MF(r) (Glipizide + Metformin)	"Decreases FPG by 74 mg/dl; PPG by 83 mg/dl"	Simonson DC et al. *Diabetes Care*. 1997 Apr; 20(4): 597-606.	*Double-blind multi-centred RCT* Glipizide 5 and 20 mg doses decreased FPG by 42 (6 and 60 (6 mg/dl from baseline; and PPG by 60 (10 and 58 (10 mg/dl respectively. Further, study pertained to monotherapy	False claim
(4)	Infen-25(r) (Dexketoprofen Trometamol)	"Offers high potency and powerful analgesia as compared to oral morphine"	[a.] Ighom G et al. *Br J Anaesth*. 2002 Apr; 88 (4): 520-6. [b.] Lopez-Munoz FJ. *J Clin Pharmacol*. 1998 Dec;38(12 Suppl:11S-21S.	[a] *Double blind RCT* No head to head trial of morphine with dexketoprofen [b] *Animal study*	Exaggeration of efficacy
(5)	Letroz(r) (Letrozole)	"Superior to CC in combined gonadotropin cycle"	Barosso G et al. *Fertil Steril*. 2006 Nov;86(5):1428-31.	*Prospective, randomised, blinded trial* Trial not designed to assess superiority of Letrozole over Clomiphene citrate (CC) but to study the efficacy of letrozole and CC as adjuvants to recombinant FSH (rFSH) in controlled ovarian hyperstimulation	Exaggeration of efficacy
(6)	Meftal Forte(r) (Mefenamic acid + Paracetamol)	"Least relative GI bleeding compared to ibuprofen and diclofenac."	García Rodríguez LA, Jick H. *Lancet*. 1994; 343 Mar 26; 343(8900):769-72.	*Retrospective case control study* The adjusted relative risk (95% CI) of GI bleed was similar for ibuprofen 2.9 (1.7-5.0) and mefenemic acid 2.9 (1.5-5.6)	False claim
(7)	Misoprost-600(r) (Misoprostol)	"Can be used in high risk patients of bronchial asthma, pregnancy-induced HTN, Rh -ve blood groups"	Rao SB et al. *Bombay Hospital Journal* .2002 Jan; 44(1): 30-5.	*Single blind, non-randomised trial* Patients with pregnancy-induced HTN were excluded in the study	False claim
(8)	Nipcare(r) (Lanolin USP Modified)	"For prevention of sore nipples, Lanolin should remain first-line therapy"	Hagen RL. *Arch Pediatr Adolesc Med.* 1999 Jun; 153(6):658.	*Comment on RCT* Comment does not state Lanolin as first line therapy. Moreover, original article corresponding to the comment advocates "In light of both the cost and the risk of infection, first-line treatment should remain breast shells and lanolin."	Misquoting of evidence
(9)	Orofer XT(r) (Ferrous ascorbate + Folic acid)	(A) "Helps to improve cognitive function, learning and memory"	Beard J. *J Nutr.* 2003 May;133(5 Suppl 1):1468S-72S.	*Review article* No independent study for improvement in learning and memory	Exaggeration of therapeutic benefit
		(B) "Negligible risk of anaphylaxis reactions"	Breymann C. *Blood Cells Mol Dis.* 2002 Nov-Dec; 29(3):506-16; discussion 517-21.	*Review article* Minimal (not 'negligible') risk of allergic accident	Exaggeration of safety
(10)	Rovamycin Forte(r) (Spiramycin)	(A) "Safety documented"	Nucera E et al. Scand *J Infect Dis* 2002; 34(7):550-1.	*Case series of 2 pregnant patients* Case series concludes further studies in a larger group of patients are needed in order to assess the safety.	False claim and unjustified generalisation
		(B) "Only antibiotic recommended in pregnancy"	Russo M, Carmellino S. *Infez Med* 1996;4(1):7-13.	*Review article* Reference does not state that spiramycin is the only antibiotic recommended in pregnancy. Moreover, Spiramycin is not approved by the US FDA and is considered as an experimental drug.	Exaggeration of safety