Influence of the legislation on the advertisement of psychoactive medications in Brazil

Influência da legislação sobre as propagandas de medicamentos psicoativos no Brasil

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Abstract

Objetive: The regulations on the advertisement of medications aim to encourage and promote an improved health care and the rational use of medications. The objective of this paper is to evaluate the influence of three regulations on the advertisement of medications: the "Export act", published in the United States in 1986; the "WHO's Criteria", published in 1988, and the Resolution 102/2000 of the Collegiate Board of Directors of the ANVISA (Agência Nacional de Vigilância Sanitária- Brazilian Sanitary Surveillance Agency), on the advertisement of psychoactive medications.

Method: We collected advertisements that were published in Brazilian psychiatric journals before and after the regulations were established. The contents of the advertisements were analyzed according to a program created based on the regulation's demands.

Results: In the 118 analyzed issues there were 199 different advertisements on 85 psychotropic drugs. We observed that, regardless the studied medication, the information about restrictions of use, such as adverse drug reactions, interactions, contraindications, warnings and precautions, does not appear very often, and when it does, its print sizes were smaller than that of the information favoring the use, such as indication, presentation and dosage. After the publication of the regulations, only 38.2% of the advertisements had all the essential technical information, and 35.3% were irregular in some way.

Conclusion: The data suggest that there was very little influence of the regulations on the advertisement of psychotropic drugs in Brazil. Consequently, other control measures are necessary in addition to the regulations.

Keywords Advertising. Legislation about drug. Legislation on medication. Psychotropic drugs.

Resumo

Objetivo: Os regulamentos sobre propaganda de medicamentos visam apoiar e fomentar a melhoria da atenção à saúde e o uso racional de medicamentos. O objetivo deste trabalho é avaliar a influência de três regulamentos sobre propaganda de medicamentos: "Export act", publicado em 1986 nos Estados Unidos; os "Critérios da OMS", em 1988 e a Resolução da Diretoria Colegiada n° 102 de 2000 da ANVISA (Agência Nacional de Vigilância Sanitária), sobre os anúncios de medicamentos psicoativos.

Método: Foram coletados anúncios em periódicos de psiquiatria nacionais, publicados antes e após cada regulamento. O conteúdo dos anúncios foi analisado de acordo com um roteiro de análise de conteúdo elaborado segundo as exigências dos regulamentos.

Resultados: Dos 118 fascículos analisados, foram obtidos 199 anúncios diferentes de 85 medicamentos psicoativos. Observou-se que, independentemente do regulamento estudado, as informações que restringem o uso, como reações adversas ao medicamento (RAM), interações, contra-indicações, advertências e precauções estão presentes em menor freqüência e num tamanho de letra menor do que as informações que favorecem o uso, como indicação, apresentação e posologia. Depois de todos os atos publicados apenas 38,2% dos anúncios continham todas as informações técnicas imprescindíveis, e 35,3% dos anúncios apresentavam alguma irregularidade.

Conclusão: Os dados sugerem que houve pouca influência dos regulamentos sobre os anúncios de medicamentos psicoativos no Brasil, portanto, faz-se necessário adotar outras medidas de controle além de regulamentos.

Descritores Publicidade. Leis sobre medicamentos. Legislação. Publicidade de medicamentos. Psicotrópicos.

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Introduction

Non-ethical promotion of medications is a major problem in most of the world, mainly in developing countries, what can generate an irrational use, and promote overprescription, self-medication and abuse.[1]

The main goal of regulations about drug advertisement is to incentive the improvement of medical care by means of a rational use of medications,[2] assuring that physicians do not provide negative consequences to their patients due to the information contained in the advertisements.

With that aim, the US Congress by means of the *EXPORT ACT of 1986* obliged the American multinational companies to provide, in the advertisements of their medications in other countries, the same information about indication and restriction of use approved by the Food and Drug Administration (FDA).[3]

Up to then, medications in the US which had not been approved by the FDA were exported and commercialized in other countries such as Brazil.[4]

In 1988, with the same goal, the World Health Organization (WHO) adopted the 'Ethical and scientific criteria for drug advertisement'. This document aimed to regulate the publications about medications for medical professionals and the public, as well as the distribution of free samples for the public, pharmacovigilance, divulging of information, content of product information sheet and labels, and conduct of advertisers.[2,4]

Among its recommendations, the advertisements of prescribed medications should include, at least, the following information: generic name, commercial name, indication, dosage and presentation, name of the excipients with known adverse drug reactions, adverse drug reactions (ADR), precautions, contraindications, warnings, main interactions, name and address of the manufacturer or distributor and adequate references.[2]

We may remind that the requisitions of the WHO are recommendations to associate countries and do not have the power of law over the State, but Brazil, as a signing member, is ethically obliged to comply.

In Brazil, a previous regulation dealing with the advertisement of medications lacked specificities and was flawed when compared to other countries, as we can see in the Executive Order 79,094 of January 5, 1977, which regulates the Act 6,360/76, in its Article X, clause 118, II – '*that the text, figure, image or projections do not insinuate false interpretations, error or confusion regarding the composition of the product, its finalities, mode of use or origin or claim non-proved therapeutical properties at the time of its registration*', and clause 118, III – '*contraindications, indications, precautions and warnings about the use of the product shall be mandatorily declared*'.

In 1978, ABIFARMA (Brazilian Association of Pharmaceutical Industries), in 1978, established its '*Voluntary Advertising Ethical Code*', aiming to guide the pharmaceutical industry of Brazil in its '*Best Practices for the Promotion and Commercialization of Medications*'.[5] According to the report of Herxheimer and Collier[6] it is widely known how the self-regulation is flawed, with no punishment for infringers.

Twenty years after the publication of the Act 6,360/76 and its executive order, the Act 9,294/96 was published, but it was only regulated by the competent agency four years later, by means of ANVISA (Brazilian Sanitary Surveillance Agency), which published in November 30, 2000 the Resolution 102 of the Collegiate Board of Directors (RDC), approving the regulation about advertisements.[7]

According to this regulation, the required information for the promotion of prescription drugs are: commercial name (when applicable), generic name, indication, posology, contraindications, precautions and warnings (including interactions and ADR). The information should be compatible with the registration in the ANVISA (clause 13, I), besides the scientific corroboration of the declared statements in the officially recognized national and international literature (clause 15).[7]

Any advertisement has an important role in the choice of the medication to be prescribed. Saporito & Goldberg[8] state that advertisement is the main source of rapid information to physicians as they use in average five minutes to obtain information about medications they prescribe due to the overload of work which reaches 50 to 60 weekly hours. Therefore, it is evident the ethical dilemma in which are involved physicians and pharmaceutics when choosing a medication in face of the practice of advertisements.[9]

Regarding psychoactive medications, the advertisement in medical specialties journals has a significant role in their divulging, as the advertisement of prescribed medications can only be performed to prescribing and dispensing professionals.[2,7]

The assessment of advertisements of psychotropics is very important, as they are the third most prescribed drugs.[10] In a recent study performed in the state of Minas Gerais, it was observed that 27% of prescriptions of a great hospital were composed by psychoactive medications.[11] Besides, studies accomplished in the '70s and the '80s stated that the advertisements of psychoactive medications tended to be less informative than those of other therapeutic classes.[12,13] Up to now, no study has assessed the influence of the country's regulations on the psychotropics in Brazil.

Therefore, knowing the quality of Brazil's advertisements of psychotropics and the impact of the regulatory acts in force is fundamental to set up national policies about medications.[14] Thus, this study tried to identify the influence of the adopted

Table 1- Regulations, date of publication and periods of data collection.

Regulations	Month of publication	Period of collection of addvertisements	
		Before	After
U.S Export Act[3]	Dec./1986	Dec./85 to Nov./86	Jan./87 to Dec./ 87
WHO's criteria[2]	May/1988	May/87 to April/ 88	June/88 to May/ 89
RDC* 102/2000 of ANVISA[7]	Nov./2000	Jan./00 to Dec./00	Jan./01 to Dec./01

**Resolution of the Collegiate Board of Directors.*

regulations and criteria for advertisement of psychoactive medications in Brazilian psychiatric journals, and to assess the content of these advertisements according to the therapeutical class.

Methods

Sample

Selection of sample periods

In order to verify the influence of regulations in the advertisement of psychotropics we collected all published advertisements before and after the implementation of each studied regulation, obtaining thus six distinct periods (Table 1).

Selection of material sources

The survey of psychotropic advertisements was performed in journals, after the establishment of the following criteria.

First, we established as an inclusion criterion advertisements originated only from medical journals, as we needed to collect advertisements since December 1985, what would be impossible if we selected other sources of advertisement of manufacturers or materials of advertisers that had been divulged more than fifteen years ago.

The second criterion was the choice of psychiatric journals, as these journals were those with more advertisements of psychotropics.[15]

The third requisite was the inclusion of journals indexed by the National Library of Medicine (List of Indexed Journals – in Index Medicus, 1999) and by LILACS (OPAS/OMS, 1997), which contained drug advertisements. Indexed journals have the advantage of an easy access to database queries, being thus the most requested and known in several parts of the country and more available at several university libraries, besides assuring the regularity of the publications for data collection purposes.

Brazilian journals which met established criteria were:

- Arquivos de Neuro-Psiquiatria (São Paulo)
- Revista de Psiquiatria Clínica (São Paulo).
- Jornal Brasileiro de Psiquiatria (Rio de Janeiro)
- Revista Brasileira de Psiquiatria (São Paulo) [former - Revista ABP-APAL].

Collection, organization and identification of the advertisements

In the 118 analyzed Brazilian issues there were 199 Brazilian advertisements of 83 psychoactive medications, which, once organized, were submitted to a detailed analysis of their content.

Analysis of content is defined as a technique to treat research data focused on an objective, systematic and quantitative description of the content of 'communications' (texts and interviews, among others). Therefore, although having originated in quantitative research, it seeks to interpret qualitative materials.[16]

We started the analysis skimming through the advertisements, which is the first contact of the analyst with the studied material, aiming to obtain 'impressions and orientations' about the material,[17] and guiding the development of the program for the analysis of content.

Program for the analysis of the content of advertisements

We developed a program for the analysis of content of advertisements based on the requirements of the regulations for the individual analysis of each advertisement. The program had the following parts:

First part – *Identification*: it had the objective of identifying *which* medication (commercial name, generic name, manufacturer and therapeutical class) and *when* (before or after the respective publication of the regulation) the advertisement was published.

Second part – *Technical content*: it aimed to identify and quantify information about indication, dosage, posology, ADR, interactions, precautions and warnings regarding: a) the presence; b) number of information per technical item; and c) emphasis each item received, given its print size.

Third part – *General aspects*: it encompasses aspects related to figures and their characteristics, sentences of impact and possible irregularities contained in the advertisements.

Data processing

Regarding data processing we developed an application, generated in the language DELPHI, for critical data entry and production of reports.

The application uses the information of the program to analyze the content of the advertisement, in which all collected

Table 2 – Frequency of advertisements of psychoactive medications analyzed according to therapeutical class and type of prescription, according to periods before and after the studied regulations.

Therapeutical Class and special control list administrative rule 344/98		American Act 22/12/1986		WHO's criteria 13/05/1988		RDC 102/2000 30/11/2000		Total	
		Before	After	Before	After	Before	After	N	%
Antidepressants	C	25	14	12	4	138	74	67	34.9
Anxiolytics	B	47	38	22	32	28	28	195	25.5
Neuroleptics	C	12	10	4	5	34	34	99	12.9
Hypnotics	B	24	7	9	9	32	11	92	12.0
Anticonvulsants	C	4	3	0	15	15	21	58	7.6
Antiparkinsonians	C	8	0	0	3	5	0	16	2.1
Mood stabilizers	C	1	1	2	0	4	0	8	1.0
Others		0	0	0	0	21	9	30	4.0
Total		121	73	49	68	277	177	765	100

Source: Revista Brasileira de Psiquiatria; Jornal Brasileiro de Psiquiatria; Revista de Psiquiatria Clínica and Arquivos de Neuropsiquiatria.

advertisements were typed meeting the program's pre-established criteria.

Each advertisement was typed in a program composed by six spreadsheets: one for identification, four for technical analysis of content and one about the general aspects of the advertisement.

The program displayed *open* spaces(allowing to type the content of advertisements without limit of words), *semi-open* spaces (allowing the typing only of numbers, such as the average number of words and print size) and *closed* spaces(allowing to fill in only already-coded and pre-established information, such as therapeutical class, type of notification, period to which pertains the advertisement).

Data analysis

Advertisements were compared regarding the presence, average of information and print size per technical item before and after each act.

Limitations of the study

We found the greatest difficulties regarding the analysis of issues of the '80s, as not all of them were complete with all their pages, what led us to more than one university library. However, all published issues were analyzed. We also found it difficult to analyze the technical content of the advertisements due to the small sizes of their prints.

Results

General characteristics of the sample

The therapeutical classes with the highest frequency of advertisements were the antidepressants, followed by anxiolytics and neuroleptics, which together corresponded to 73.3% of Brazilian advertisements (Table 2). Analyzed advertisements came from 39 industries, being 15 of them Brazilian and 24 foreign.

The number of substances that were announced as having antidepressant properties had the greatest increase in the last years, what is explained by the appearance of the class of the serotonin and noradrenalin inhibitors. The same occurred with antipsychotic substances and the new atypical neuroleptics which became the third most announced therapeutical class.

However, in the studied sample only 16% of announced medications are essential. According to the WHO's program, essential medications are those deemed safe, efficient, with acceptable quality and low price. Brazil's Health Department, by means of its executive order 3,916 of 1998, which established the Brazilian policy of medications, also recommends the promotion and the use of Brazil's essential medications list (RENAME) (Administrative rule 507/99), based on the WHO's list.[14]

Influence of regulations on the content of advertisements of psychoactive medications

Technical content of advertisements

A – American act

In the studied period, there were only three products of American manufacturers that were advertised on Brazilian psychiatric journals. None of them had neither information about drug interactions nor the manufacturer's address to allow the requisition of information, both before and after the passing of the American Act.

Even though we knew that the American act has not legal power on Brazilian advertisements of non-American compa-

Table 3 – Presence of most frequent technical information according to the periods before and after the regulations on advertisements of psychoactive medications.

Technical Information	American Act dec/1986		WHO's criteria May/1988		RDC 102/2000 Nov./2000	
	Before N (%)	After N (%)	Before N (%)	After N (%)	Before N (%)	After N (%)
Indications	37 (94.8)	31 (100.0)	18 (94.7)	19 (100.0)	57 (95.0)	33 (97.0)
Presentation	35 (89.7)	30 (96.7)	18 (94.7)	17 (89.5)	40 (66.6)	28 (82.3)
Posology	26 (66.6)	26 (83.8)	19 (100.0)	17 (89.5)	35 (58.3)	28 (82.3)
Generic name	34 (87.2)	29 (90.3)	17 (89.5)	18 (94.7)	51 (85.0)	34 (100.0)
Manufacturer	34 (87.0)	28 (90.0)	6 (31.7)	19 (100.0)	58 (96.5)	34 (100.0)
Total of addvertisements	39 (100.0)	31 (100.0)	19 (100.0)	19 (100.0)	60 (100.0)	34 (100.0)

Table 4 – Presence of least frequent technical information analyzed according to the periods before and after the regulations in advertisements of psychoactive medications.

Technical Information	American Act Dec/1986		WHO's criteria May /1988		RDC 102/2000 Nov./2000	
	Antes N(%)	Depois N(%)	Antes N(%)	Depois N(%)	Antes N(%)	Depois N(%)
Adverse drug reations	20 (51.3)	20 (64.5)	10 (52.6)	10 (52.6)	22 (36.6)	25 (73.5)
Warnings	20 (51.3)	22 (70.9)	10 (52.6)	12 (63.2)	21 (35.0)	26 (76.3)
Interactions	20 (51.3)	21 (67.7)	9 (47.3)	11 (57.8)	22 (36.6)	25 (73.5)
Contraindications	20 (51.3)	20 (64.5)	10 (52.6)	12 (63.2)	22 (36.6)	25 (73.5)
References	6 (15.4)	7 (22.6)	8 (42.1)	9 (47.4)	33 (55.0)	20 (58.8)
Complying advertisements	4 (10.2)	5 (16.2)	6 (31.6)	5 (26.3)	8 (13.2)	13 (38.2)
Total of addvertisements	39 (100.0)	31 (100.0)	19 (100.0)	19 (100.0)	60 (100.0)	34 (100.0)

nies, we chose to analyze all published advertisements in this period, as there was a world-wide discussion about the quality of prescribed drug advertisements. Besides, we decided to maintain this global form to allow possible comparisons with other regulations analyzed in this study.

In these periods, most frequent data found were indications, posology, presentation, generic name and manufacturer's name (Table 3), whereas the least frequent were those that somehow restricted the use such as ADR, interactions, warnings and contraindications (Table 4).

Of note, the American act had no influence on Brazilian advertisements, as expected (as before this act there were four advertisements who presented all necessary technical information and after its publication this number raised to five complying advertisements (Table 4).

Regarding the content of information about possibly-quantifiable technical items, we observed that the information about ADR and drug interaction has increased (Table 5), although still appearing at footnotes or in attached pages, in small print.

B – WHO's criteria

After the establishment of the WHO's criteria there have been few changes, except for the manufacturer's name, which has started to be present in all advertisements (Tables 3 and 4).

Table 5 shows that the content of technical information has remained almost unchanged, except for two advertisements which had more episodes of ADR after the establishment of the WHO's criteria. Of note, top extreme values remained unchanged, except for one advertisement that had nine ADR after the publication of the WHO.

Regarding the emphasis given to technical items, the information which facilitates the prescription of the medication (prescription and posology) is presented in print sizes bigger than that restricting the prescription (warnings, contraindications, ADR and interactions).

C – RDC 102/2000

After 12 years of the WHO's recommendations and after the publication of the RDC 102/2000, information about indications, presentation and posology is still more frequent than that about ADR, interactions, warnings and contraindications (Tables 3 and 4).

The scientific basis that drug advertisements should present is still hardly frequent, i.e., only slightly more than half (58.8%) of advertisements analyzed after the publication of the RDC had bibliographic references (Table 4). Of these, one third did not belong to indexed journals or to officially recognized references and two thirds belonged to scarcely representative sources, such as manufacturer's books and protocols, non-indexed journals, bulletins of associations, non-published studies presented in meetings and oral presentations in seminars, congresses or meetings of specialists.

The decrease of about 50% in the advertisements (60 advertisements before and 34 after the implantation of the RDC - Table 3), has coincided with an increase in the percentage of all information, what could be explained by the fact that less informative advertisements stopped being published. Anyway, advertisements started to comply more with the proposals of the resolution: 8 (before) and 13 (after) advertisements complied - Table 4).

Regarding the content of ADR and drug interactions data, they appeared more in the advertisements (Table 5). Despite the increase in the content of these data, there is a growing distance between the advertisement and the information page. The summary of the drug information sheet was rarely presented at the advertisement's footnote, and was mostly presented in pages distant from the advertisement page, in hardly legible print that ended not even being seen by the journal's reader.

Data favoring the prescription, such as indications, posology and presentation, were still being presented in print size quite bigger than restricting ones such as ADR, interactions, warnings and contraindications. We noted that the greater the content of technical information the smaller the print size.

Irregularities present in the advertisements

We have considered as irregularities all information that the regulations reported as forbidden and all and any statement that was subjective or had not had officially recognized references, according to the WHO and RDC 102/2000 criteria.

Some of these irregularities found in Brazilian advertisements were:

Inadequate indications

'It gives you back your tranquility and restores the equilibrium'; 'equilibrium restored', 'single dose of tranquility'; 'it gives you back the natural way of life'; 'tranquility with simplicity'; 'a light for your patients'.

Table 5 – Median of the Quantity of technical information of each technical item analyzed in Brazilian advertisements before and after the regulations in advertisements of psychoactive medications.

Technical Information	American act Dec./1986		WHO's criteria may /1988		RDC 102/2000 Nov./2000	
	Before Md. (extr)**	After Md. (extr)**	Before Md. (extr)**	After Md. (extr)**	Before Md. (extr)**	After Md. (extr)**
Indications	2 (1-18)	2 (1-19)	1,5 (1-6)	1 (1-6)	1 (1-20)	2 (1-20)
Adverse drug reactions	4 (1-50)	7 (2-50)	3 (1-8)	6 (1-9)	13,5 (3-76)	16 (3-76)
Interactions	2 (1-7)	4 (1-9)	2 (1-9)	2 (1-9)	4,5 (1-18)	6 (1-20)
Warnings	5 (1-12)	5,5 (3-14)	6 (4-12)	7,5 (4-12)	8,5 (1-16)	9 (4-16)
Contraindications	2 (1-8)	2 (1-8)	2 (1-5)	2 (1-5)	2,5 (1-7)	3 (1-15)
Total of advertisements	39	31	19	19	60	34

**Md (extr) = median (extreme values)*

Approved/ reliable

'You trust in it, you prescribe it', 'reliable for a higher number of patients'; 'successful due to its use', 'The anxiolytic that the medical community has approved'.

Standard or reference medication

'Standard antidepressant', 'world leader in the treatment of insomnia'; 'WHO's reference anxiolytic'; 'first choice' 'high efficacy standard'.

Approved by responsible agencies

'Approved by the FDA and Brazil's Health Department'.

Absence of interactions

'Does not interact with other medications'; 'does not interact with alcohol'.

The most prescribed one

'The most prescribed anxiolytic', 'for being the most prescribed anxiolytic it needs to have something more'.

Quick answer

'Rapid beginning of action'; 'rapidness with lower sedation'; 'rapidness and efficacy in depression, panic and OCD'; 'immediate relief'.

Suggestion of a wide spectrum

'An anxiolytic which meets all needs'; 'great range of action'; 'wide solution'; 'efficient in all forms of depression', 'Wherever anxiety might hide or is manifested'.

Physiological action

'The right physiological sleeping'; 'the most physiological of inductors'.

Certainty of efficacy

'Certainty of efficacy'.

Pharmacokinetics

'Superior pharmacokinetics *for a better life'*.

After the publication of each regulation we noted a decrease in the number of irregularities, although none of the regulations was enough to terminate them (Table 6).

Discussion

General aspects of classified advertisements

In the '80s (before and after the American act and the WHO's criteria), the most prevalent advertisements were those of *anxiolytic* and hypnotic medications while from 2000 to 2001 advertisements of antidepressant prevailed. Similar data were observed in one study, in which advertisements of psychotropics in medical journals in Nordic countries had been analyzed for 20 years. This study named the advertisements from years 1975 to 1985 as the 'Age of sleeping pills' and those from the middle of the '90s onwards as the 'Age of antidepressants'.[18]

We found that the promotion of psychoactive medications by pharmaceutical industries is similar in several countries, regardless their epidemiological situations. In Brazil, for example, the prevalence of psychiatric disorders does not exceed 10.2%.[19] Of note, thus, the lack of engagement of manufacturers in the demands of the country in which the product is commercialized, i.e., it is as if the need of a medication came before the epidemiological need.

Or else, advertisements could have been favoring a higher number of diagnoses and treatments of certain diseases, therefore altering the epidemiological profile of the region in which the medication is available. It is believed that this phenomenon could have occurred in the '80s with anxiolytic and hypnotic medications and more recently with antidepressants, as the latter have been submitted to a wider and less adequate utilization in all senses, reaching nearly to the idea of a psychiatric panacea.[20]

Influence of regulations on the advertisements of psychoactive medications

The American act (1986) was not sufficient to improve the quality of advertisements. It is believed that the indifference regarding this act might have occurred due to the lack of control of the Brazilian government and to the lack of examina-

Table 6 – Frequency of irregularities found in the advertisements of psychoactive medications before and after the studied regulations.

	Total	Export Act 99,660 Dec./1986		WHO's criteria May/1988		RDC 102/2000 Nov./2000	
		Before (13 months)	After (12 months)	Before (6 months)	After (12 months)	Before (13 months)	After (12 months)
Subjective indications	26	10	5	4	5	2	0
Approved/Confidence	15	1	1	0	0	7	6
Reference / Standard	12	1	2	0	0	4	5
Approved by FDA/ MS/ APA	11	0	0	0	0	7	4
Without interaction with other drugs	6	2	1	1	2	0	0
The most prescribed one	5	0	0	0	0	3	2
Quick response	5	2	3	0	0	0	0
Wide spectrum	4	1	0	1	0	1	1
Physiological action	4	1	0	1	1	1	0
Certainty of efficacy	2	0	0	1	1	0	0
Pharmacokinetics	1	0	0	0	0	1	0
Irregular advertisements/ Total of advertisements	12/39	8/31	6/16	7/19	19/60	12/34	

tion by the headquarters of American companies of the promotional materials divulged in Brazil.

There have not been great changes in the content of advertisements published in psychiatric journals after the publication of the WHO's criteria (1988). This lack of adherence to the regulation might be explained by the criteria being only recommendations to associated countries and not having the power of law. However, Brazil, as a signing member, was obliged to comply and to enforce the regulation. The non compliance with the WHO's criteria might have occurred due to a flaw in their divulging or still due to the omission of Brazilian sanitary agencies.

The publication of the RDC 102/2000 reinforced the same requirements that had been already established 12 years before by the WHO's criteria (1988). However, we observed that the Brazilian regulation had an impact on the advertisements of psychoactive medications, as it regulation halved the number of advertisements published in the psychiatric journals (the 60 advertisements published before the RDC were reduced to 34 after it – Table 3), and half of Brazilian manufacturers canceled their circulating advertisements.

Actually, the impact of the RDC was not necessarily related to the improvement in the quality of advertisements, as only 38.2% of them complied with the regulation after its publication, but to the cancellation of less complete advertisements. This fact is evident when analyzing the items that restrict the prescription (ADR, interactions, warnings and contraindications); therefore, before the RDC only 22 out of 60 advertisements (35%) had these items; after the RDC the number of advertisements decreased to 34, of which 25 had these items (73.5%).

Nevertheless, the regulation is thought to have had a positive impact. It is believed that out of the three studied regulations, only the RDC had a positive impact on the advertisements, perhaps because it is a Brazilian regulation and therefore more easily divulged and controlled in the country than the others.

Summing up: regardless the studied period, the most frequent and most highlighted data due to their print size were the ones that favored the prescription: indications, posology and presentation, whereas the less frequent and less important information were those restricting the prescription of the medication such as ADR, drug interactions, contraindications and warnings.

Similar finding were also observed in other promotional sources. Pizzol et al[21] who analyzed pieces of medication advertisement distributed to physicians in two cities of the state of Rio Grande do Sul observed that 73% of them presented the posology in larger print sizes than those of general precautions which were present in only 43% of the collected material.

The same occurs in other countries; in Russia, less than 10% of advertisements contain precautions, contraindications and drug interactions and 2% had bibliographic references.[22] In Argentina, 100% of the material of advertisers had no information about drug interactions, contraindications, ADR and precautions; 46% of the references were incorrect and we could not find them; and 69% of them were difficult to access as they were from other countries.[23]

We might speculate, thus, that in promotional materials which are divulged by other mass media, the flaws in the information are still higher than those found in indexed journals.

Although the bibliographic references have increased their frequencies in advertisements along the years, less than 60% of advertisements published in 2001 had them and one third had non-indexed references. The fact that medication advertisements lack informative and scientific character is considered a severe irregularity, according to the criteria of several regulatory agencies.[24-26]

Irregularities

The most frequent irregularities were related to subjective indications. After the publication of the three regulatory acts, 35.3% of the advertisements still had some irregularity.

Subjective indications reinforce erroneous concepts and prejudices of society. Carlini[10,13] found that, in Brazil, women were overrepresented in advertisements of psychoactive medications, and generally had diffuse and apparently unmotivated illnesses; on the other hand, when the figure was a man, indications for the use of the medication were due to tension, excess of responsibility or of work.

The stereotyped image of emotive, irrational and complaining women, presented in anxiolytic advertisements, leads to overmedication, to the so-called 'housewife syndrome', mainly for 'nervous conditions' and 'insomnia', making them receive 60% more of any medication, with a greater difference for the cases of anxiety, depression, tension and insomnia.[27]

Women figures were much more common in the advertisements of anxiolytics, being the male/female ratio 1:2, the same found by Noto et al[28] who analyzed the prescriptions of benzodiazepines in two cities of the state of São Paulo. The authors found that women were prescribed twice anxiolytics than men. The irrational appeal of advertisements is reflected in the medical prescription, leading to a bias between mental disorders and gender.[29]

Besides female figures, the use of metaphors is not rare, i.e., symbols which perform a direct association with the product: owls, rainbows, dolls, animated pills, butterflies, etc. Lion,[30] when presenting advertisements of medications to physicians without giving their names, observed that those which contained metaphors were more recognized than the others.

Anyway, the use of benzodiazepines is high in the Brazilian population. According to a survey in the state of Rio Grande do Sul, the prevalence of use of benzodiazepines is 46.7%,[31] i.e., almost half of the population have already used at least once in their lifetime this therapeutical class.

On the other hand, advertisements of neuroleptic medications used much more male figures (6:1), usually adult and aged men. In this case it is suggested that aged men were stereotyped as having psychotic disorders. The same was observed by Riska & Huggund,[32] when analyzing the advertisements of neuroleptic medications in medical journals of Nordic countries.

Schizophrenia and other psychoses are much less common among elderly people; however, in the U.S. 750,000 people

aged above 65 receive antypsychotic drugs, and the estimated prevalence of schizophrenia among the elderly for whom there would be the need of using neuroleptics is near to 92,000 people.[33] Besides, the advertisements of neuroleptics deal with the product's confidence and security mentioning its time in the market and mainly the millions of patients who had already used the medication.[24] We observed that the process of medicalization and stereotyped representation of mental disorders in drug advertisements occurs all over the world.

The advertisements of psychotropics even use a scientific language but their messages tend to have a marketing language, presenting messages of autonomy, satisfaction and plenitude.[34]

Deceitful messages were observed in advertisements of antidepressants suggesting a rapid effect for the treatment of panic disorder, from two to three weeks. Studies claim that the start of response to the antidepressive treatment occurs, at least, after 15 days. In the treatment of panic disorders, the effects appear after two to eight weeks and the beginning of withdrawal of the medication, after six months to one year of treatment. For obsessive-compulsive disorder (OCD) 12 to 26 weeks of medication are recommended.[35]

A launching advertisement of a hypnotic medication claimed that one out of two people had already had difficulties to sleep and informed that an innovatory medication would be soon reaching the market. Indeed, the incidence of complaints about insomnia is high in the population.[36] However, insomnia can stem many times from other comorbities, such as psychiatric disorders and respiratory problems, situations in which the use of hypnotics should be avoided. Besides, simple measures, called as 'sleep hygiene' should be adopted: avoiding caffeine and naps after the meals and the performing of regular physical activities can help the therapy of insomnia, making unnecessary the use of hypnotics.[37]

Mood stabilizers, medications for the treatment of the syndrome of alcohol and tobacco abstinence and the acetylcholinesterase inhibitors, besides some antidepressants launched in the market, did not contain any technical information, being those the classes which disagree more with the studied regulatory acts.

The irregularities most commonly found by the agencies responsible for the assessment of medication advertisements and in studies assessing the already-published promotional materials,[23,26,38-43] were:

- Purposeless scientific studies;
- Non-published references;
- Difficult access to the quoted scientific articles;
- Incorrect statistical package;
- Incorrect methodologies;
- Results bias;
- Non-proved experimental data;
- Omission of unfavorable reports;
- Omission of failure rates;
- Failure to inform the consequences of use;
- Selection of some precautions and warnings and omission of some data from the original drug labeling;
- Presence of unnecessary information such as FDA approval;
- Suggestion of incorrect doses regarding the mentioned clinical study;
- Dangerous conclusions, extrapolations and percentual projections in a small sample;
- Vaguely-described qualifications of safeness, effectiveness and superiority (one of the most observed in this study);
- Brief's summary's drug labeling and advertisement displayed in different pages.

Jaillon (2000)[26] reports that out of 9,000 advertisements that are annually registered by French manufacturers, only in 1% of them there is no need of further change before the divulging.

Despite the advance in the regulations, such as the RDC 102/2000, published by ANVISA in Brazil, we do not have yet a system for the analysis of medication advertisements as the FDA and the French agency. A possible consequence of this failure is expressed in one study performed in the '80s which, when analyzing advertisements of prescribed medications in Brazil, had reported that the advertised material had used flawed statistics and methodology, 'scientific studies' with biased samples, lack of a control group, small experimental groups and non-statistically significant diferences.[44]

It would be interesting to perform further studies, twenty years after Victora's data[44], in order to verify the current situation, adding to these data the quality of bibliographic references, what could not be performed in our study.

The implantation of any of the regulations did not suffice to prevent the irregularities in medication advertisements. Up to day old irregularities are still occurring and new ones have appeared. Actually, what has happened was an increase in the types of irregularities.

Conclusions

1. Assessing the influence of the three studied regulations – the American act ('Export act'), WHO's criteria and the RDC 102/2000-, we concluded that the only one that promoted some impact on medication advertisements was the RDC 102/2000. Actually, the number of inadequate published articles decreased by fifty percent. However, this regulation, as the others, was not enough to enhance the quality of the technical content of the remaining advertisements, as less than half (38.2%) of them had all requested technical information and 35.5% still had at least one irregularity;
2. Despite the advances in the regulations with the publication of the RDC 102/2000, the same flaws and the mode of arranging the information which were already present since the first years of the study (1986) were still present. That is, the information which favors the prescription (such as indications, presentations and posology) is the most frequent and is still presented in print size greater than that which restricts it (such as ADR, medication interactions, contraindications, precautions and warnings);
3. In the year which preceded the publication of the RDC 102/2000, 55% of advertisements had bibliographic references and after its publication they have not exceeded 58.8%. However one third of them were references of protocols

and materials from the manufacturer itself, non-indexed journals, bulletins of associations, and not-published congress presentations. This suggests that further studies are needed to assess the methodological quality and the content of the references cited in the drug advertisements;

4. We observed inadequate advertisements such as: suggestion of start of effects in advertisements of antidepressants; suggestion of pharmacist treatment for all types of insomnia in an advertisement of a hypnotic; omission of information regarding the maximum treatment period in all advertisements of anxiolytics and the omission of mandatory warnings in advertisements of neuroleptics. These failures are deemed irregularities, according to the clauses 4 and 13 of the RDC 102/2000;
5. There are still inadequate and subjective indications for psychoactive medications, such as, *'it solves the problems without creating others'*, or *'the antidepressant which brings life back in its best expression'* hinting a solution for the daily problems, what has been observed since the '70s and may generate an overmedicalization for diffuse and emotional illnesses;
6. Female figures are more frequent in advertisements of benzodiazepines and antidepressants; on the other hand, male figures are more frequent in advertisements of neuroleptics, favoring a stereotype between gender and psychiatric disorders, suggesting that anxiety and depression are female and young symptomatologies, whereas schizophrenia and other psychoses are male and elderly symptomatologies, therefore indirectly influencing the medical conduct;
7. Data suggest that most of pharmaceutical industries do not have a commitment with the Brazilian policy of medications regarding the priority to promote essential psychoactive medications, as less than 16% of the advertisements were of medications with this classification;
8. Our findings suggest that other measures are needed besides the regulations, such as educational programs promoted by ANVISA directly for pharmaceutical manufacturers and health professionals. A direct line with associations such as the ABP (Brazilian Psychiatric Association) should be also created, and these associations, after an adequate analysis of the advertisements, would file denounces to ANVISA against inadequate advertisements;
9. Journals of medical specialties should reassess their conduct regarding advertisements. For example, not allowing the publication of the brief summary's drug labeling in illegible print size or else that this summary and the advertisement be in different pages and distant from the advertisement.
10. The implantation of disciplines in the program content of Medical and Pharmacist schools enabling these professional to perform a critical analysis of the material of drug promotion or the possibility of performing specialization courses to already-graduated physicians and pharmacists with the same finality. This discipline or course should aim to train professionals for the critical and methodological analysis of scientific studies (perception of sample errors, of the extrapolation of *in vitro* data as if they were *in vivo* ones or experimental as if they were clinical ones, analysis of the adequacy of statistical packages) and to warn them against the possible stereotypes of medication advertisements comparing them with epidemiological data.

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