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IMPACT OF EDUCATIONAL INTERVENTIONS ON ADVERSE DRUG EVENTS REPORTING

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Introduction: Spontaneous adverse drug events (ADE) reporting is the main source of data for assessing the risk/benefit of drugs available in the pharmaceutical market. However, its major limitation is underreporting, which hinders and delays the signal detection by Pharmacovigilance (PhV).
Objectives: To identify the techniques of educational intervention (EI) for promotion of PhV by health professionals and to assess their impact.
Methods: A systematic review was performed in the PUBMED, PAHO, LILACS and EMBASE databases, from November/2011 to January/2012, updated in March/2013. The strategy search included the use of health descriptors and a manual search in the references cited by selected papers.
Results: 101 articles were identified, of which 16 met the inclusion criteria. Most of these studies (10) were conducted in European hospitals and physicians were the health professionals subjected to most EI (12), these studies lasted from one month to two years. EI with multifaceted techniques raised the absolute number, the rate of reporting related to adverse drug reactions (ADR), technical defects of health technologies, and also promoted an improvement in the quality of reports, since there was increased reporting of ADR classified as serious, unexpected, related to new drugs and with high degree of causality.
Conclusion: Multifaceted educational interventions for multidisciplinary health teams working at all healthcare levels, with sufficient duration to reach all professionals who act in the institution, including issues related to medication errors and therapeutic ineffectiveness, must be validated, with the aim of standardizing the Good Practice of PhV and improve drug safety indicators.

Keywords: pharmacovigilance, adverse drug reaction reporting systems, education continuing, educational intervention, health knowledge, attitudes, practice

A systematic review showed that one of two hospital admissions may be arising from adverse drug events (ADEs) (1). A same prevalence of occurrence of adverse drug reactions (ADRs) can be observed during the length of hospital stay of inpatients (2); however, only 6 percent of them are reported (3). This proportion is far below than that one recommended by the World Health Organization, which targets the number of 250 reports per million of inhabitants (4). Therefore, underreporting decreases the sensitivity of the passive method of vigilance, hindering and delaying the assessment of risk/benefit of the drugs available on the pharmaceutical market.

Despite of this limitation, the spontaneous reporting systems provide high volume of information at a low cost and their most important function is the early detection of a signal (hypothesis regarding a causal relationship between the use of a drug and the development of ADR). The voluntary reports of ADE are done, mainly, by health professionals, especially physicians (5), pharmacists (6), and nurses (7). When the minimum and desirable fields for ADE are filled in the yellow card (or another specific document, because the safety drugs polices vary from country to country), this information helps to prevent and/or decrease the occurrence of ADR, medication errors and ineffective treatment, as well as to contribute to the quality of the drugs (8). Therefore, it is necessary to develop strategies that contribute to the promotion of pharmacovigilance by multidisciplinary teams in healthcare institutions.

General educational interventions (EI) have been demonstrated as an effective method applied to change the health professionals' behavior/attitude (9), because the main reasons of underreporting (ignorance, diffidence, lethargy, indifference, and complacency) (10) are demonstrated, the appropriate concepts and practices of pharmacovigilance are explained and the correct fill of forms are elucidated. Therefore, EI contribute to decrease the lack of knowledge among the reporters and to increase the awareness regarding the importance of this service in health institutions. Consequently, there is an improvement in the adherence of nurses, pharmacists and physicians in the service, resulting in the increment of the problems reporting related to safety, quality, and effectiveness of health technologies (11).

In this context, the present study aimed to identify the techniques of educational interventions used to promote pharmacovigilance in healthcare institutions by health professionals and to assess their impact on ADE reports.

METHODS

A systematic review was performed in PUBMED, PAHO, LILACS, and EMBASE computerized databases, between November of 2011 and January of 2012, updated in March/2013, to identify original studies that assessed the impact of educational interventions to encourage spontaneous reporting of ADE by health professionals.

The strategy of search was carried out according to PRISMA Statement(12). The following health descriptors were

used for data collection: "education, continuing" OR "education, medical" OR "intervention" OR "health knowledge, attitudes, practice" AND "adverse drug reaction reporting systems" OR "adverse drug reaction reported spontaneously" AND "pharmacovigilance". A manual search was also performed in the references of selected articles to look for relevant studies that might not be identified by the health descriptors used (STEP 1).

A first screening of all articles identified was carried out, with a view to exclude review manuscripts, editorials, letters, news, abstracts of conference proceedings, data from thesis/dissertations, and original studies published in journals indexed in the databases consulted which were not written in English, Portuguese, or Spanish languages (STEP 2).

The selected articles were reviewed and those which did not perform educational interventions for health professionals to promote spontaneous reports of ADE in healthcare institutions and did not assess their impact were excluded from the present study. Included manuscripts were independently reviewed by two authors (C.P., F.R.V.) (STEP 3). Quality assessment of the manuscripts was not carried out. Disparities were resolved by discussion.

The extraction of the following variables of interest was performed: (i) design of the study; (ii) target group; (iii) workplace (level of health care where the educational interventions were carried out, corresponding to: primary [family physicians, pharmacies and drugstores]; secondary [outpatient clinics]; and tertiary [hospitals]); (iv) duration of the educational interventions; (v) techniques developed and applied; (vi) the impact on ADE reporting; and (vii) country where the study was performed.

The impact on ADE reporting was assessed in terms of the quantitative and qualitative parameters that were compared before and after the educational interventions. The quantitative impact was identified as the increase in the absolute numbers, percentages or rates of ADE reports after the educational intervention. The qualitative impact was observed as the increase in the absolute numbers, percentages or rates of reports of ADR classified as serious, unexpected, with a high degree of causality and related to new drugs on the market after the educational interventions.

RESULTS

Using the search strategy in computerized databases and manual search (STEP 1), a total of 101 articles was identified (Figure 1). After the initial screening, twenty-six were selected to be reviewed (STEP 2). Of these, sixteen met the inclusion criteria (4,13–27) (STEP 3); and ten were excluded (28–37) (Table 1).

The designs of the eligible studies were longitudinal (six randomized controlled trials, five quasi-experimental, two case-control studies, two ecological time series analysis, one observational analytic), with duration ranging between 1 month and 2 years. A breakdown by geographical region showed that fourteen studies were conducted in Europe. In general, the physician was the main professional involved in the educational interventions ($N = 12$) and tertiary health care was the preferred level to carry out the interventions ($N = 11$). The educational interventions techniques frequently developed in the studies were: distribution of educational material or repeated sending of emails ($N = 14$); presentations - lectures, workshops, group dynamics, periodic meetings and outreach visits ($N = 10$) and interviews or questionnaires ($N = 8$) (Table 2).

Regarding the impact of educational interventions, most studies ($N = 12$)(4,13–23) showed an increase in the absolute numbers, percentages or rates of the spontaneous reports of ADR (including those considered serious, unexpected, with a high degree of causality and related to new drugs) and technical defects of health technologies. Two studies assessed only quantitative impacts (24,25); one showed only qualitative impacts (26); and the other one did not show significant differences in the indicators evaluated (27) (Table 2).

Table 1. Articles Excluded after Content Analysis and the Reason for Exclusion

Author (year)	Reason for exclusion
GERRITSEN et al. (2011)	EI was not developed for health professionals, but for students.
BANIASADI et al. (2008)	EI conducted for health professionals, but it did not assess the impact.
BÄCKSTRÖM et al. (2007)	EI conducted for nurses, but it did not assess the impact.
DURRIEU et al. (2007)	EI was not developed for health professionals, but for students.
GRANAS et al. (2007)	EI conducted for pharmacists; however, it did not assess the impact.
BACKSTROM et al. (2006)	Economic intervention conducted without EI.
COX et al. (2004)	No one EI was developed.
ROSEBRAUGH et al. (2003)	EI was not developed for health professionals, but for students.
MORRISON-GRIFFITHS et al. (2003)	EI conducted for nurses, but it did not assess the impact.
GOLDMAN et al. (1999)	EI conducted for health professionals, but it did not assess the impact.

Note. EI, educational intervention.

DISCUSSION

Pharmacovigilance-based educational interventions showed positive impacts (quantitative and qualitative) on ADE spontaneous reporting by health professionals in twelve studies analyzed, which adopted multifaceted techniques for interventions, including: lectures, placement of yellow cards, distribution of

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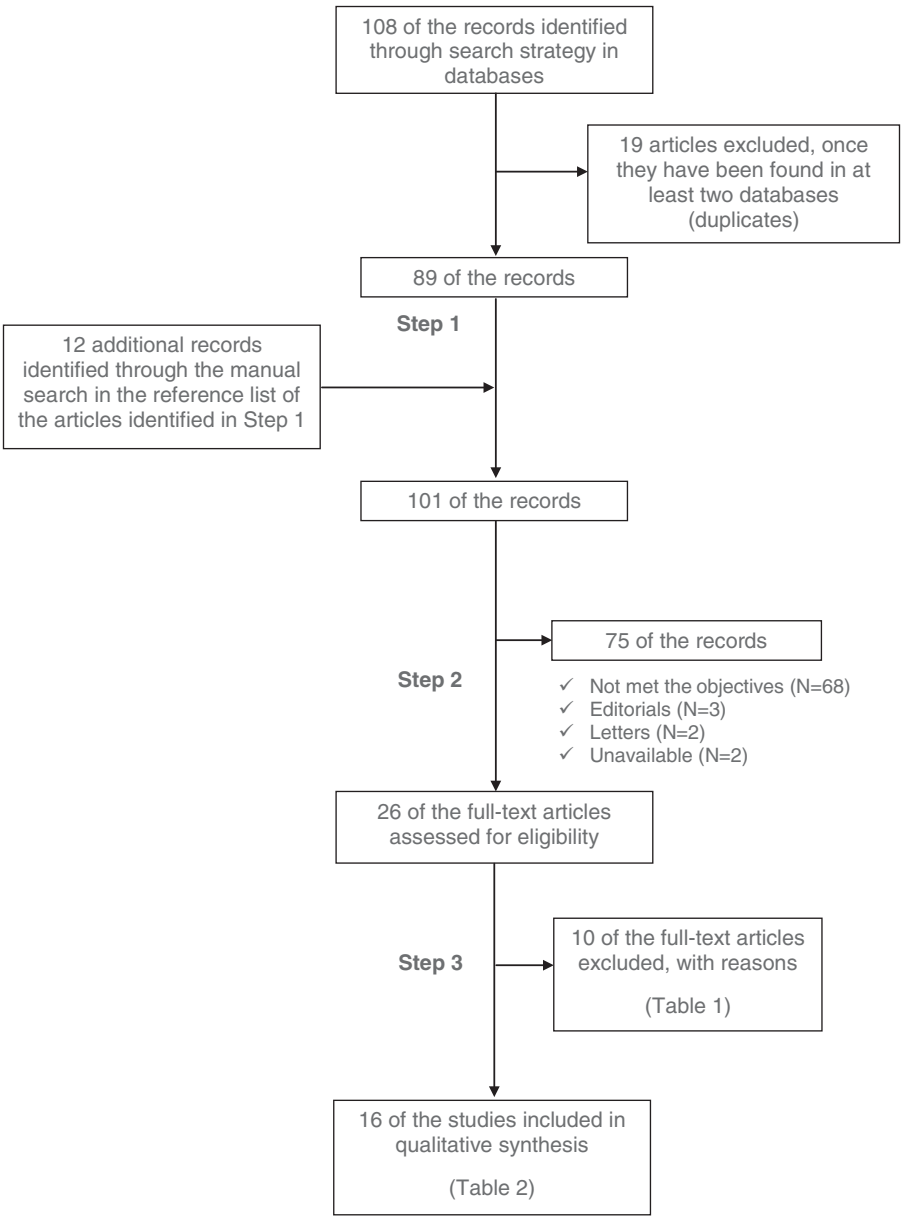

Figure 1. Flowchart of article selection process for systematic review on ADR reporting, adapted to The PRISMA Statement.

printed educational materials and giveaways, as well as the organization of workshops. The strategies adopted contributed to the adherence of health professionals to pharmacovigilance activities, changing the behavior/attitude of the employees toward the reporting of suspicions of problems related to safety and quality of health technologies. These findings corroborate the data of a systematic review performed by Forsetlund et al. (9), whose authors noted that general interventions (not related to ADR reporting/vigilance) developed for health professionals which apply multifaceted techniques are more effective in changing their behavior/attitude than single strategies.

Two studies applied only one technique in the educational intervention – repeated sending of emails (24,27). However, just one showed a quantitative impact on ADR reporting (24). The difference may be explained due to the major frequency of EI technique carried out by the Italian group (they sent an email with a brief newsletter on drug safety, once a month, for 10 months) (24) when compared with the work performed by the Swedish group (they sent an email, three times in a year, with information regarding the importance of ADR report) (27). This finding suggests the importance of continuing education for health professionals to improve ADR reports.

The assessment of educational interventions' impact by the absolute numbers of ADE reports has an important limitation, because this indicator does not take several factors into account that may increase or decrease these numbers. Therefore, the safety indicators may be overestimated. For example, the rise in the absolute number of spontaneous reports of ADE may

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Table 2. Description of the Countries, Level of Healthcare, Methods, and Educational Interventions' Impact of the Studies Published in the Databases PUBMED, PAHO, LILACS, and EMBASE, from November of 2011 to January of 2012, Updated in March of 2013

Educational intervention methods							
			Duration (month)				
Study design	Target group (*N*)	Workplace	EI	Follow-up	Techniques	Results	Author (year)/country
Cluster-randomized controlled trial	Physicians ($N = 6,579$)	Tertiary Secondary	-	After EI: 20	1) Workshops or telephone interviews 2) Distribution of educational materials	- Workshop: the spontaneous ADR reporting rate increased (RR 3.97; 95% CI 3.86,4.08), as well as the report rate of serious ADRs (RR 6.84; 95% CI 6.69, 6.98) and for high-causality ADRs (RR 3.58; 95% CI 3.51, 3.66) - Telephone interviews: less efficient, but they also improve ADR reporting (RR 1.02; 95% CI 1.00,1.04).	HERDEIRO et al. (2012) Portugal
Cluster-randomized controlled trial	Physicians Nurses ($N =$ not mentioned)	Primary	12	-	1) Repeated distribution of educational material	- There was not observed significant difference between the mean numbers of ADR reports *per* unit in case group (1.03 ± 2.46) and control group (0.70 ± 1.21). However, the mean number of high quality reports *per* unit was grater in the case group (0.47 ± 0.94) than the control group (0.20 ± 0.57).	JOHANSSON et al. (2011) Sweden
Cluster-randomized controlled trial	Pharmacists ($N = 364$)	Tertiary Primary	1	After EI: 20	1) Telephone interviews 2) Workshops 3) Distribution of educational material	-The rate of ADR reporting *per* 1000 pharmacists-month in the case group increase (RR 3.22; 95% CI 1.33;7.80), including ADR classified as: severe (RR 3.87; 95% CI 1.29;11.61); unexpected (RR = 5.02; 95% CI 1.33, 18.93), when compared with the control group.	RIBEIRO-VAZ et al. (2011) Portugal
Cluster-randomized controlled trial	Pharmacists ($N = 117$)	Primary	12	Before EI: 12	1) Repeated sending of emails (3 times/year)	- The proportion of units reporting ADRs did not differ between the intervention and the control group (49 vs. 52%). -The proportion of high-quality reports did not differ between groups.	JOHANSSON et al. (2009) Sweden
Cluster-randomized controlled trial	Pharmacists ($N = 1,433$)	Tertiary Secondary Primary	4	Before EI: 12	1) Group dynamics 2) Distribution of educational material	The rate of ADR reporting *per* 1000 pharmacists-year increase (RR 5,87, 95% CI 1.98,17.39), including ADR classified as: serious (RR 9.79, 95% CI 2.24, 42.66); high-causality (RR 8.67, 95% CI 2.12, 35.42); unexpected (RR 4.41, 95% CI 1.11, 17.53) and new-drug related (RR 9.33, 95% CI 2.53, 34.40)	HERDEIRO et al. (2008) Portugal

Educational intervention methods							
			Duration (month)				
Study design	Target group (*N*)	Workplace	EI	Follow-up	Techniques	Results	Author (year)/country
Cluster-randomized controlled trial	Physicians (N=6,541)	Tertiary Secondary	5	After EI: 11	1) Educational outreach visit 2) Distribution of educational material (reminder cards, yellow card placement)	- The rate of ADR reporting per 1000 physicians-year increase (RR 6.32, 95% CI 3.81, 27.51), including ADR classified as: serious (RR 6.32, 95% CI 2.09, 19.16); high-causality (RR 8.75, 95% CI 3.05, 25.07); unexpected (RR 30.21, 95% CI 4.54, 200.84) and new-drug related (RR 8.04, 95% CI 2.10, 30.83)	FIGUEIRAS et al. (2006) Portugal
Quasi-experimental	Health professionals (*N* = 737)	Cites no healthcare level	10	Before EI: 4 After EI: 10	1) Repeated sending of emails (10 times in 10 months)	The overall number of reports coming from the intervention group increased by 49.2%, while the number of reports coming from the control groups increased by 8. 8%.	BIAGI et al. (2013) Italy
Quasi-experimental	Physicians Pharmacists Nurses (*N* = not mentioned)	Tertiary	4	After EI: 12	1) Lectures 2) Workshops 3) Distribution of educational materials, reminders 4) Giveaways	- Spontaneous reports increased by 225% in the first EI; 146% in the second EI; 471% in the third EI and 284% after the fourth EI.	PRIMO and CAPUCHO (2011) Brazil
Quasi-experimental	Nurses (*N* = 117)	Tertiary	12	-	1) Lectures 2) Questionnaires	- The EI resulted in at least a 10-fold increase in the ADR reporting rate (*per* 1000 hospital admission-year)	BÄCKSTRÖM et al. (2002) Sweden
Quasi-experimental	Physicians Pharmacists (*N* = not mentioned)	Tertiary	12	-	1)Sending educational material (reminder cards, update letter and a spare yellow card)	1 year after EI: 95 reports were received compared to 40 for the previous year; 15% of the ADRs reported were considered medically significant.	CLARKSON et al. (2001) England
Quasi-experimental	Physicians (*N* = 193)	Tertiary	24	-	1)Telephone interview 2)Questionnaires 3)Distribution of reminders 4) Yellow card placement	- EI led to an approximate 5-fold increase in reports, being 40% serious ADRs.	McGETTINGAN et al. (1997) Ireland
Quasi-experimental	Physicians (*N* = not mentioned)	Cites no healthcare level	24	-	1)Telephone interview 2)Distribution of educational materials 3)Questionnaires	- The absolute number of reports increased more than 17-fold. - Significant increase in the number of reports of serious ADRs.	SCOTT et al. (1990) USA

Table 2. Continued

Educational intervention methods							
			Duration (month)				
Study design	Target group (*N*)	Workplace	EI	Follow-up	Techniques	Results	Author (year)/country
Case-control	Physicians (*N* = not mentioned)	Tertiary	1 - 2	Before EI: 12 After EI: 12	1) Visits 2) Collection of reports made	- Total ADR reporting rate (number of reports/number of beds) in the two case groups increase, respectively, from 3% to 25% and from 11% to 40%. -40% of ADR after the EI was classified as severe. No significant difference was observed in the control group.	GONY et al. (2010) France
Case-control	Physicians Pharmacists (*N* = 3,784)	Cites no healthcare level	12	Before EI: 12	1) Distribution of educational material 2) Questionnaire 3) Awards	- The proportion of ADR reporting by physicians and pharmacists of case groups increase, respectively, 131% and 92%. - The proportion of appropriate ADR reported by physicians and pharmacists of case groups increase, respectively, 181% and 130%. - The increase in reporting by physicians and pharmacists of case group was significantly greater than that seen in the control group.	BRACCHI et al. (2005) Wales
Ecological time series analysis	Physicians (*N* = not mentioned)	Tertiary	24	Before EI: 48	1) Periodic educational meetings 2) Distribution of educational material (memory-cards) 3) Economic incentive	- The proportion of spontaneous ADR reporting increase from 29.5% to 71.5%. - The proportion of serious cases reported increase from 32.5% to 63.1%).	CEREZA et al. (2010) Spain
Ecological time series analysis	Physicians (*N* = not mentioned)	Tertiary	24	Before EI: 48	1) Periodic educational meetings 2) Distribution of educational material (reminder cards) 3) Economic incentive	- The proportion of spontaneous ADR reporting increase from 29.5% to 71.5%. - The proportion of serious cases reported increase from 32.5% to 63.1%).	PEDRÓS et al. (2009) Spain

Note. EI, educational intervention; ADR, adverse drug reaction; RR, relative risk; CI, confidence interval.

be related to the inauguration of new wards or to the recruitment of new employees in the health institutions. Therefore, the improvement in the number of ADE reports might not be associated, necessarily, with the educational interventions.

Most interventions ($N = 11$) were conducted at the tertiary healthcare level. This is a good strategy in countries where the health professionals work in different levels of healthcare services (primary/secondary and tertiary), because the knowledge and attitudes acquired in educational interventions at the hospital can cover a larger geographic area, improving the surveillance of different drugs. However, the conduction of EI is necessary in all healthcare levels (drugstores, pharmacies, offices, ambulatories, and hospitals), with the purpose of stimulating the passive vigilance, the detection of ADE and to contributing for the assessment of drug safety and the regulation of pharmaceutical market.

Physicians were frequently included in the educational interventions identified ($N = 12$). In Europe, these professionals contribute with the most of the ADR reports received by Pharmacovigilance Centers (38); indeed, some international programs of drug monitoring, for example the Swedish program, do not allow ADR reporting by pharmacists and nurses (39). The reason for this approach may be the belief that doctors, because they are the professionals responsible for the diagnosis, perform ADR reports of better quality (8).

All studies were conducted in countries that are members of the official World Health Organization (WHO) Program for International Drug Monitoring, which demonstrate the concern of these nations to raise the compliance of the health professionals to the pharmacovigilance service and to achieve the target number of ADR reports recommended by WHO. Therefore, the rates of underreporting would be minimized, allowing accurate evaluation of the safety, quality and effectiveness of available health technologies on the pharmaceutical market.

Regarding the duration of educational interventions, it was noted that those of longer duration aimed to cover larger numbers of employees of the institutions to increase the health professionals' adherence and participation in the study, and to contribute to safety drug analysis. Besides, the periods established for the monitoring of ADE spontaneous reporting were useful to demonstrate the need for continuing education, because the numbers and rates of reports tended to be equal to those in the period before intervention, that is to say, a few months after the application of the educational intervention techniques. Therefore, Ribeiro-Vaz et al. (4) recommend the periodic updating of professionals, to keep them aware about the importance of reporting the suspicion of ADE.

Limitations of the Study

Data may be underestimated, owing to selection bias, because just four databases were consulted and only articles written in Spanish, English and Portuguese were analyzed. Consequently, some other pharmacovigilance educational interventions carried out to improve ADE reporting may not have been identified by the methodology adopted in this study. Furthermore, the quality assessment of the eligible manuscripts was not carried out. Therefore, the reliability of the findings demonstrated in the systematic review should be evaluated with caution.

CONCLUSION

Educational interventions for the promotion of pharmacovigilance by health professionals should: (i) be directed at a multidisciplinary health team and include issues related to ADR, technical defects of health technologies, medication errors and ineffective therapy; (ii) use multifaceted techniques with: lectures, group dynamics (to practice correct filling of yellow card), distribution of educational material and certificates; (iii) continue for the length of time needed to reach most professionals in the health institution (this variable depends on the size of the establishment staff); (iv) be conducted at all levels of health care to reach different patients and drugs, making it possible to assess the attributes of safety, quality and effectiveness of most drugs available in the public health sector, and (v) be offered periodically, with the view to update the health professionals in the pharmacovigilance service.

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CONFLICTS OF INTEREST

All authors report they have no potential conflicts of interest.

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