Effectiveness of pharmacovigilance: multifaceted educational intervention related to the knowledge, skills and attitudes of multidisciplinary hospital staff

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OBJECTIVES: Most educational interventions in pharmacovigilance are designed to encourage physicians to report adverse drug reactions. However, multidisciplinary teams may play an important role in reporting drug-related problems. This study assessed the impact of a multifaceted educational intervention in pharmacovigilance on the knowledge, skills and attitudes of hospital professionals.

METHOD: This prospective, open-label, non-randomized study was performed in a medium-complexity hospital in São Paulo, Brazil. The intervention involved four activities: 1) an interactive lecture, 2) a practical class, 3) a pre-post questionnaire administered to professionals on a multidisciplinary team, and 4) educational material. The intervention’s impact on the professionals’ knowledge and skills was assessed using the World Health Organization’s definitions. The intervention’s effect on the professionals’ attitudes was analysed by the prevalence of adverse drug event reports (adverse drug reactions, medication errors, therapeutic failure and drug quality deviations) and the relevance (seriousness and expectancy) of the events.

RESULTS: One hundred seventy-three professionals were enrolled. A 70-fold increase in the number of adverse drug event reports was observed during the 12 months post-intervention. The intervention improved the professionals’ form-completion skills ($p<0.0001$) and their knowledge of pharmacovigilance ($p<0.0001$). The intervention also contributed to detecting serious drug-induced events. The nursing staff reported medication errors, and pharmacists and physiotherapists recognized serious adverse drug reactions. Physicians communicated suspicions of therapeutic failure.

CONCLUSIONS: A multidisciplinary approach to drug-safety assessments contributes to identifying new, relevant drug-related problems and improving the rate of adverse drug event reporting. This strategy may therefore be applied to improve risk communication in hospitals.

KEYWORDS: Pharmacovigilance; Health Knowledge; Attitudes; Practices; Interventional Studies; Product Surveillance.

INTRODUCTION

Although the limitations of traditional systems designed to detect adverse drug events (ADEs) are well known (1), spontaneous reporting remains the cornerstone of post-marketing drug safety surveillance (1,2).

The use of spontaneous reporting persists because new approaches that have been developed to improve risk com-
Although the contributions of Latin American countries to the field of pharmacovigilance has increased in recent years, a minority of Latin American nations invest in professional training. Therefore, biases in epidemiological communication and impairments in signal detection result from the lack of robust information available during the post-marketing life cycle of drugs.

Several strategies have been implemented to promote adherence to appropriate pharmacovigilance practices among health professionals in pharmacovigilance services, and these have primarily involved designing educational interventions, including subjects related to drug safety assessments in both undergraduate and postgraduate programs, and increasing the amount of time dedicated to teaching pharmacovigilance in universities. The most important objective of these educational interventions is to develop functional and behavioural competencies to promote changes in attitude among physicians and pharmacists towards adverse drug reaction (ADR) reporting. These educational interventions do not include other types of ADEs, such as medication errors, therapeutic failure and drug quality deviations. Consequently, drug-induced harm is underreported.

Given the constraints of healthcare assistance in low- and middle-income countries (brief contact between physicians and patients, lack of time to report drug-related problems and lack of information in patients’ records about drug safety), the responsibility for ADEs must be shared among trained healthcare professionals (pharmacists, nurses) to decrease underreporting. However, studies of multidisciplinary teams are scarce in the literature.

Based on these considerations, the current study aimed to 1) assess the impact of a multifaceted educational intervention (MEI) on the prevalence of ADE reporting (attitude) by multidisciplinary teams, 2) evaluate the effectiveness of the MEI on professionals’ knowledge of and skills in pharmacovigilance and their fulfilment of ADE reporting requirements, and 3) assess the degree of relevance of the ADE reports submitted after the MEI according to the events’ seriousness and likelihood of occurrence.

## MATERIALS AND METHODS

### Study population and setting

The study was conducted in a medium-complexity, general and public hospital with 94 beds. The hospital is located in the Araraquara-São Carlos region (São Paulo State, Brazil), which comprises 24 municipalities and includes over one million inhabitants. The hospital is known for providing healthcare for infectious diseases and neurologic rehabilitation (approximately 13,000 appointments per month).

The inclusion criteria comprised all hospital staff (physicians, pharmacists, nurses, auxiliary nursing and pharmacy staff, and administrative officers, as well as social assistants, physiotherapists, audiologists, nutritionists, psychologists, and occupational therapists) with an employment link to the hospital who agreed to participate by signing an informed consent form. The exclusion criteria included professionals who were on sick leave or vacation, those who were not eligible to participate in the intervention and those who declined to respond to the questionnaire despite having shown interest in the intervention by participating in the lecture and practical class.

### Design of the study

A longitudinal, prospective, open-label and non-randomized study using a single group before-and-after intervention design was conducted from 1 February 2012 through 31 May 2012. A before-and-after design measures the performance of one or more subjects after the introduction of an intervention to assess the intervention’s effect.

Although randomized controlled trials represent the most suitable research design for evaluating the effectiveness of an intervention, we were unable to design a randomized controlled trial due to the unavailability of an appropriate control group. Therefore, we opted to use the before-and-after design due to its simplicity and its robustness relative to observational research. Furthermore, findings in the literature have demonstrated the positive impact of educational interventions in pharmacovigilance on changing the behaviour of health professionals. Additionally, because the introduction of an intervention may improve risk communication, we decided that ethical principles could not be satisfied if a control group was unable to benefit from the acquisition of knowledge regarding drug safety assessments through the intervention.

### Multifaceted educational intervention

The applied MEI model was first proposed by Pagotto et al. (2013). To assess the reproducibility of the method, a pilot study was conducted in six hospital institutions in Mucuripe member countries. Briefly, the MEI involved four different activities: a lecture on pharmacovigilance concepts and the landscape of pharmacovigilance; a practical class on how to correctly complete ADE reports; the distribution of educational materials and the administration of a questionnaire to the participating professionals before and after the MEI. These activities were conducted during four separate sessions, each of which lasted one hour.

In the first session, the pre-test assessment was administered via questionnaire. The instrument’s development and the determination of its constructs and constructs of interest were based on the literature. The questionnaire included three sections: the first section related to knowledge assessment (five essay questions about the importance of pharmacovigilance), the second section focused on attitudes (five essay questions related to ADE reporting), and the final section consisted of an evaluation of the professional’s skills regarding information that is considered essential, necessary and unnecessary on an ADE report. This portion of the study was designed to obtain baseline data about the hospital staff members’ knowledge, skills and attitudes related to pharmacovigilance.

The second and third sessions involved lectures, a practical class, and the distribution of educational material to multidisciplinary teams of hospital staff. The post-test assessment was conducted during the final session. The participants were asked to fill out the same questionnaire they completed in the first session to enable an evaluation of the effectiveness of the intervention on their knowledge, skills and attitudes.

### Follow up and outcome measures

The knowledge assessment was performed by analysing the responses to the questionnaire; each item on the questionnaire was assigned a score ranging from 0–10. The World Health Organization’s definitions for pharmacovigilance (21)
Table 1 - Criteria considered to be gold standard in terms of knowledge [32] and skill [2] assessment in pharmacovigilance.

| KNOWLEDGE                                                                 | GOLD-STANDARD ANSWERS                                                                 | SKILLS                                                                 | GOLD-STANDARD ANSWERS |
|---------------------------------------------------------------------------|---------------------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------|
| 1) What is pharmacovigilance?                                            | The monitoring of medicine use for the detection, assessment and prevention of adverse drug reactions and any issues related to medicine. | 1) ADR reporting                                                      | About the patient: name, medical record number, bed, gender, clinical history (illness, comorbidities, drug allergies). |
| 2) Does the practice of pharmacovigilance promote benefits? When positive, what are the benefits and who are the beneficiaries? | The practice of pharmacovigilance promotes benefits for drug users, professionals and healthcare institutions. The benefits include contributing to patient safety, improving the quality of care in health facilities, and ensuring that drugs on the pharmaceutical market are safe, effective and high quality. | About ADR: clinical manifestation (treatment initiation and finalization), evolution (outcomes), laboratory tests, treatment (hospitalization, discontinuation of drugs, prescription of drugs). | About the suspected drug: drug, dose, route of administration, indication, date of treatment initiation and finalization, expiry date, lot number and manufacturer. |
| 3) Who may notify?                                                       | Drug users, health professionals and the pharmaceutical industry.                      | About medication errors reporting                                      | About the reporter: name, profession, telephone number or e-mail and date that the report was made. |
| 4) What can you notify?                                                  | Any drug-related problems, especially adverse drug reactions, medication errors, therapeutic ineffectiveness and drug-quality deviations. | 1.2) Desirable criteria                                                 | About the patient: risk factors for ADR occurrence (kidney and/or hepatic failure, previous exposure to the drug, alcohol consumption or a smoking habit). |
| 5) What do you mean by:                                                   |                                                                                       |                                                                        |                        |
| a) Adverse drug event?                                                   | Any damage or harm caused to patients arising from drug use.                           |                                                                        |                        |
| b) Adverse drug reaction?                                                | A response to a drug that is noxious and unintended that occurs at doses normally used in humans for prophylaxis, diagnosis, therapy of disease, or for modifications to physiological function. | About the ADR: clinical evolution (outcomes), documentation of diagnoses (including procedures applied, data from laboratory tests and pharmacological treatment). |                        |
| c) Medication errors?                                                    | Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. | 2) Medication error reporting                                           |                        |
| d) Quality drug deviations?                                              | A departure from the quality parameters established for a product or process. In pharmacovigilance, these deviations can include organoleptic changes that are either physico-chemical and/or general (leaks, inadequate labelling, foreign particles, etc.). | 2.1) Desirable criteria                                                | About the product: the product involved in the error (dose, route of administration, expiry date, lot number, type of packaging, label, etc.). |
| e) Suspicious of therapeutic ineffectiveness?                            | The total or partial absence of the expected effect of the drug on the condition of use prescribed or indicated in the leaflet. |                                                                        | About the place: where the error occurred (appropriateness to carrying out the activities, promotes distractions, considerable noise, etc.), medical equipment and products used (meet the attributes of quality and safety), service flow, etc. |
| 6) What is the correlation between pharmacovigilance and drug safety?    | The practice of pharmacovigilance, monitoring drug use, contributes to the regulation of the pharmaceutical market because it focuses on the safety, quality and effectiveness of these products. |                                                                        | About the person involved: characterize regarding time of graduation, time of employment, duty period, aetiological causes and contributing factors. |
| 7) How would you explain why a drug does not produce the desired effect? | The medicine may not produce the desired effect for three primary reasons: the inherent characteristics of the patient, medication errors and quality deviation. |                                                                        |                        |
| 8) In which stages of drug use can medication errors occur?              | In all stages: prescribing, dispensing and administration.                              |                                                                        |                        |

were considered gold-standard answers (Table 1). Scores below 5 were considered unsatisfactory, scores between 5 and 7.5 were considered average and scores above 7.6 were considered satisfactory in terms of knowledge acquisition.

The skills evaluation was based on the professionals' perception of the degree of relevance of the information reported on an ADE form. Accordingly, the professionals were asked to highlight the ADE form fields according to whether the data required for those fields are considered unnecessary, necessary or essential. The minimal and desirable criteria to be supplied in an ADE form were defined according to the recommendations of the Pan-American Health Organization (22) (Table 1). The Wilcoxon-Mann-Whitney statistical test was used to assess the impact of the MEI on the participants' knowledge and skills. Statistical significance was set at p < 0.05.
To analyse the impact of the MEI on the attitudes and behaviour of the participating professionals, the absolute number of ADE reports (ADR, therapeutic failure, medication errors and quality deviations) 12 months prior to the intervention (t0) were investigated. A year of follow up regarding the absolute number of ADEs reported post-intervention was also performed (t2) to assess changes relative to t0.

The Mann-Whitney statistical test was used to identify significant differences between the proportions of the number of ADE reports/the number of hospitalized patients before the educational intervention (t0) and after the educational intervention (t2). An evaluation of the effectiveness of the MEI on ADE reporting was performed using segmented generalized linear regression models. Adjustment segmentation was conducted by including a variable that represented the period over which the MEI occurred (t1).

The relevance of the ADR and medication error reports made during the study period was also evaluated (seriousness and expectancy of occurrence). The seriousness of medication errors was assessed according to the standards of the National Coordinating Council for Medication Error Reporting and Prevention (23). Serious ADRs were defined as those causing hospitalization, those that were fatal or life-threatening, or those that resulted in significant changes in patient treatment (thereby prolonging hospitalization) (24). Informational drug sheets approved by the National Agency of Sanitary Surveillance (ANVISA) and monographs, such as those in the DRUGDEX (MICROMEDEX® database), UpToDate® database and LexiComp Manole (2009), were consulted to verify the expectancy of an ADR.

Table 2 - Adherence of hospital staff and the impact of educational interventions on knowledge related to pharmacovigilance and skill filling out forms related to adverse drug events according to professional classification (N=173). Américo Brasiliense-SP (Brazil).

| Professional                  | Adherence | Number employed (N) | Return rate (N) | Knowledge | Impact | p-value |
|-------------------------------|-----------|---------------------|----------------|-----------|--------|---------|
|                               | Answered the questionnaire (N) | Before Mi (min-max) | After Mi (min-max) | p-value | Before Mi (min-max) | After Mi (min-max) | p-value |
| Physicians                    | 11        | 86                  | 12.8           | 4.3 (2.9-6.6) | 5.0 (0.4-9.3) | 0.006* | 4.0 (0.0-7.9) | 5.2 (0.0-9.2) | 0.007* |
| Multidisciplinary team        |           |                     |                |           |                    |                    |         |
| Social assistant              | 4         | 5                   | 80.0           | 3.9 (1.3-5.4) | 6.3 (4.8-9.3) | <0.0001* | 5.2 (3.8-6.2) | 6.1 (4.7-7.9) | <0.001* |
| Pharmacist                    | 1         | 2                   | 50.0           | 4.8 (NA) | 5.9 (NA) | 0.0 (NA) | 0.0 (NA) | 0.0 (NA) |         |
| Physiotherapist               | 10        | 12                  | 83.3           | 2.1 (1.0-6.0) | 5.8 (4.3-9.2) | 5.4 (3.1-7.7) | 6.8 (4.5-7.7) |         |
| Audiologist                   | 2         | 4                   | 50.0           | 1.2 (0.1-2.4) | 6.2 (4.8-7.6) | 6.7 (6.2-7.2) | 5.0 (2.9-7.1) |         |
| Nutritionist                  | 5         | 5                   | 100.0          | 3.0 (2.0-3.7) | 5.8 (4.6-7.4) | 5.7 (5.3-6.7) | 7.5 (7.4-8.3) |         |
| Psychologist                  | 3         | 4                   | 75.0           | 2.7 (2.1-3.4) | 6.2 (6.0-7.8) | 5.2 (4.9-6.2) | 6.1 (4.1-7.7) |         |
| Occupational therapist        | 4         | 4                   | 100.0          | 2.0 (1.4-3.7) | 5.5 (3.2-5.7) | 4.7 (0.0-6.4) | 4.7 (0.0-6.8) |         |
| Auxiliary in pharmacy         | 9         | 11                  | 81.8           | 1.5 (0.0-3.1) | 5.9 (4.0-7.1) | 2.2 (0.0-6.5) | 6.7 (0.0-9.2) |         |
| Administrative officer        | 5         | 11                  | 45.4           | 0.6 (0.0-1.6) | 5.8 (3.9-7.0) | 5.8 (4.3-7.0) | 5.2 (0.0-6.9) |         |
| Nursing staff                 |           |                     |                |           |                    |                    |         |
| Nurse                         | 26        | 58                  | 44.8           | 3.3 (0.7-5.2) | 5.5 (2.2-7.7) | <0.0001* | 4.9 (0.0-7.2) | 6.0 (0.0-8.9) | <0.0001* |
| Auxiliary nurse               | 93        | 219                 | 42.5           | 2.0 (0.0-5.9) | 5.4 (0.5-8.1) | 2.0 (0.0-8.0) | 5.0 (0.0-9.2) |         |
| TOTAL                         | 173       | 421                 |                | 2.3 (0.0-6.6) | 5.2 (0.9-9.3) | <0.0001* | 3.9 (0.0-8.0) | 5.2 (0.0-9.2) | <0.0001* |

Note:
Mi=median
Mn=minimum
Max=maximum
NA=not applicable.
*Significant value.
linear regression model, the MEI significantly contributed to the increase in the number of ADE reports ($p=0.0005$).

Regarding the period of effectiveness of the MEI, a decrease of 2.5% (3.9% compared with 1.4%) was noted in the prevalence of ADEs reported four months after the MEI was implemented (Figure 1). However, the ADE reporting rate did not return to its pre-intervention level. Subsequent increases in the prevalence of ADE reporting (3.4% and 3.5%) (Figure 1) occurred due to the implementation of policies regarding risk management and patient safety at the institution.

Serious ADRs were reported by pharmacists (N=6) and physiotherapists (N=1). The nursing staff submitted the most ADE reports (150), followed by pharmacists (N=29), physicians (N=6) and auxiliary nursing staff members (N=3). The professional classification of twenty-six professionals who reported ADEs could not be determined. Medication errors (N=136) and quality deviations (N=10) were often reported by the nursing staff, whereas ADRs (N=14) were reported by pharmacists, and therapeutic failures (N=5) were reported by physicians.

A broad spectrum of medication errors were reported after the MEI, whereas no ADEs related to medication errors were reported prior to the MEI (Figure 2). Administration errors were the most frequently identified errors (Figure 2), and these related mainly to the delayed intake of a drug (N=23).

Two of the 26 ADR reports were of poor quality, as they lacked information regarding the suspicious drug associated with the event and the time of the onset of the event. The remaining 24 ADR reports were well documented, which enabled the detection of 29 clinical manifestations likely induced by 19 different drugs. With the exception of four events, whose likelihood of being drug-related was remote (alternative causes may explain these events), all the events were expected ADRs. Seven of these were considered serious for the following reasons: increased hospital stay (N=4), temporary disability (N=2) and induced hospitalization (N=1).

**DISCUSSION**

This study indicates that using MIEs with multidisciplinary teams has a positive effect on the awareness of hospital staff with respect to the importance of ADE reporting. An increase exceeding 100% in the absolute number of reports of drug-induced events was observed in the current research. The strategies applied in the intervention improved the participants’ knowledge of pharmacovigilance and increased their skills in correctly filling out report forms, primarily in relation to medication errors. Therefore, including hospital professionals in pharmacovigilance services may contribute to patient safety (25) by stimulat...
are inextricably linked in efforts to follow up on drug safety and treatment effectiveness in hospitals.

The tradition of pharmacovigilance is a recent arrival in Latin America, and there are few publications related to pharmacovigilance (2). Additional studies are necessary to assess the impact of ADE in low- and middle-income countries (5). Consequently, our educational initiative is relevant to efforts endeavouring to motivate volunteers to increase post-marketing surveillance, decrease underreporting, address the new trends derived from legislation and contribute to learning about ADE.

Limitations of the study

The findings of this study should be considered in the context of the study’s two primary design limitations. First, randomized controlled trials are considered the gold standard for evaluating the effectiveness of an intervention. However, before-and-after intervention designs are ideal if conducting a randomized controlled trial is either logistically or ethically not possible. Second, during the follow-up period for the MEI’s effectiveness, a policy regarding risk management and patient safety was deployed in our hospital. However, the implementation of this policy did not involve providing hospital staff members with training related to pharmacovigilance activities.

The MEI implemented for hospital staff in this study improved the relevance of ADE reports and increased the prevalence of such reports. Furthermore, the MEI was effective at enhancing awareness (knowledge) of pharmacovigilance, even among individuals who did not complete all the intervention protocols or return the questionnaire. This MEI can motivate the members of a multidisciplinary...
team to change their behaviours/attitudes and can contribute to improving the team members’ skills in detecting new and relevant ADEs. Therefore, the inclusion of hospital staff in drug safety analysis is an important strategy to decrease ADE underreporting and improve the communication risks associated with drug use.

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**AUTHOR CONTRIBUTIONS**

Varallo FR, Planeta CS and Mastroianni PC conceived and designed the study and were responsible for the data analysis and interpretation, and manuscript writing. All of the authors approved the final version of the manuscript.

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