Undergraduate education in pharmacovigilance is effective to develop core competencies to assess drug safety by health professionals?

Varallo FR[1], Mastroianni PC[2]
1 PhD. Pharmacist. Professor of School of Pharmaceutical Sciences of Ribeirão Preto. Universidade de São Paulo. Ribeirão Preto (SP) (Brazil)
2 PhD. Pharmacist. Adjunct Professor. Department of Drugs and Medicines. Universidade Estadual Paulista (UNESP). Araraquara (SP) (Brazil)

Fecha de recepción: 15/02/2020 - Fecha de aceptación: 20/02/2020

Ponencia presentada en "Simposio la Enseñanza de la Farmacovigilancia en las Universidades" Servicio de Farmacovigilancia del HNC – Facultad de Ciencias Médicas de la Universidad de Córdoba – Argentina – 10 de mayo 2019.

SUMMARY
Lack of knowledge, skills, and attitude in pharmacovigilance contributes to worsening drug-related morbidity and mortality and impairing the causality assessment of adverse drug reactions (ADR). The lack of ability of health professionals to identify and recognize ADR hinders the detection of risk factors, alternative causes, confounders variables, and patients more susceptible to drug-induced harm. Underreporting and incomplete reports of ADR (low quality information) still comprise the major obstacle to pharmacovigilance, even after decades of effort to improve the situation. Continuing education for health professionals is encouraged in the third global challenge of the World Organization (WHO) and is necessary to improve and innovate the teaching method of pharmacovigilance in the curricula of health courses. The curriculum should include active teaching methodologies, hands-on exercises, and current topics such as pharmacogenetics. Clinical aspects may be summarized in five key aspects importance of pharmacovigilance, identification, management, prevention and reporting. The objective is to develop proactivity in pharmacovigilance activities so that predict the risk and prevent drug-induced harm, as well as produce reports with enough information that enable signal generation and causality analysis.

Key Words: **Patient safety, education, continuing, drug-related side effects and adverse reactions, pharmacovigilance.**

¿La educación de pregrado en farmacovigilancia es efectiva para desarrollar competencias básicas a los profesionales de la salud para evaluación de la seguridad medicamentosa?

RESUMEN
La falta de conocimiento, habilidades y actitudes en farmacovigilancia contribuye al empeoramiento de la morbilidad y mortalidad relacionadas con los medicamentos y compromete la evaluación de la causalidad de las reacciones adversas a los medicamentos (RAM). La falta de habilidad de los profesionales de la salud para identificar y reconocer las RAM dificulta la detección de factores de riesgo, causas alternativas, variables de confusión y pacientes más susceptibles al daño inducido por medicamentos. Incluso, después de décadas de esfuerzos para mejorar la señal, se observa que el principal obstáculo son las notificaciones con información insuficiente, incompleta y de baja calidad. Se motiva la educación continua para los profesionales de la salud en el tercer desafío global de la Organización Mundial (OMS) y se alienta a promover e innovar el método de enseñanza de la farmacovigilancia en los planes de estudio de los cursos de salud. Se sugiere que los planes de estudio incluyan metodologías de enseñanza activa, ejercicios prácticos y temas actuales, como la farmacogenética. Los aspectos clínicos se pueden resumir en cinco aspectos importantes: importancia de la farmacovigilancia, identificación, manejo, prevención y notificación. El objetivo es desarrollar proactividad en las actividades de farmacovigilancia para predecir el riesgo y prevenir el daño causado por los medicamentos, además de producir informes con información suficiente para permitir la generación de señales y el análisis de la causalidad.

Palabras clave: **Seguridad del paciente, educación continua, efectos colaterales y reacciones adversas relacionadas con medicamentos, farmacovigilancia.**

Fabiana Rossi Varallo ◆ Av. do Café, s/n ◆ Vila Monte Alegre, Ribeirão Preto ◆ 14040-900 SP/ Brasil
varallo.f.r@gmail.com

The importance of pharmacovigilance is well documented in the literature[1]. Its benefits include the oversight and regulation of the pharmaceutical market, the evaluation of drug safety, effectiveness and quality, as well as the promotion of appropriate use of health technologies[1]. However, undergraduate pharmacy and medical students feel insufficiently trained to perform activities related to drug safety, despite of the relevance of the topic[2].

Consequently, human resources are not able to attend social and market demands regarding the detection, management, prevention and notification of adverse drug reactions (ADR). Therefore, pharmacovigilance does not contribute for health promotion, protection and recovery, since health professionals did not develop skills and attitudes related to drug safety.

Lack of knowledge, skills, and attitude in pharmacovigilance contributes to worsening drug-related morbidity and mortality and impairing the causality assessment of ADR, which should consider the entire context of the patient being treated, besides the suspected drug[3].

The lack of ability of health professionals to identify and recognize ADR hinders the detection of risk factors, alternative causes, confounders variables, and patients more susceptible to drug-induced harm[3]. It also makes difficulty the opportunities to learn from mistakes, develop risk minimization plans[4] and strategies to improve patient safety throughout the drug's life cycle.

The iatrogenic cascade is a typical example of the lack of awareness of health professionals in recognizing and managing ADR. Prescribing cascade comprises the prescription of a new medicine to treat undesirable effects of drugs[5], being common among older people with chronic illness and with polypharmacy[6].

It is important to highlight that the management of ADR may include drug withdrawal, dose adjustments, the prescription of other pharmacological treatment[7], hospitalization, supportive or palliative care, depending on its seriousness. However, inappropriate prescribing cascade occurs when an ADR is misinterpreted as a new clinical condition[5], resulting in the prescription of unnecessary pharmacotherapy, which has a potential to induce harm itself.

Consequently, the patient may develop negative clinical and humanistic outcomes due to delayed of appropriate treatment and unrequired medication. In addition, the occurrence of the iatrogenic cascade may favor the increase of economic burden[8] to health facilities, since it is a preventable event.

Clinical support tools might alert prescribers of potential iatrogenic cascade occurrence[6]. However, these technologies do not eliminate pharmacotherapeutic review. This service allows the assessment of needs of patients and can contribute for elaborating and implementing deprescribing protocols of non-required therapies or reducing the dose of essential drugs, to prevent the ADR[6].

Underdiagnose of ADR and the prescription of inappropriate drugs to older people are causes of hospital admissions[9]. The lack of awareness and resoluteness of primary attention in identifying drug-induced harm and monitoring drug safety post-commercialization overload tertiary healthcare[11]. Meta-analysis showed that one in ten hospitalizations of elderly is related to ADR, most of which are preventable[10].

The inclusion of clinical aspects in the pharmacovigilance curriculum could minimize these problems. This need is ratified by students and professionals involved in this area, mainly for the prevention of ADR[12]. Another reported subtopic was risk communication and spontaneous reporting[12].

The main purpose of ADR reporting is learning. Thus, there is a possibility to identify and know the weaknesses of the processes of drug use and then, to perform risk management and mitigation actions. In general, ADR reporting allows avoiding injuries to the clinical condition of patients, because of the characterization, even of near misses[13], which also generate extra hospital costs due to rework.

Spontaneous ADR reporting also contributes to ensuring bioethical principles, safeguarding the rights of: i) patient autonomy; ii) nonmaleficence (as already established by Hippocrates, first do no harm); iii) beneficence (maximize the benefits of care and minimize the occurrence of risks) and iv) justice[13].

However, underreporting and incomplete reports of ADR (low quality information) still comprise the major obstacle to pharmacovigilance, even after decades of effort to improve the situation[14]. A bibliographic survey identified that lack of knowledge is one of the main factors that lead to low adherence of health professionals in the communication of ADR[15].

Continuing education for health professionals is encouraged in the third global challenge of the World Organization (WHO) to minimize the occurrence of drug-induced harm, mainly those caused by medication errors[16]. Studies show that in-service education is effective to stimulate hospital health professionals to ADR reporting[17]. However, the impact is limited to four months[18], requiring periodicity of interventions.

One limitation that may explain this feature is that the content addressed in the interventions does not include the clinical aspects of ADR, causality analysis, counterfeit, quality deviations, medication errors and strategies that allow the recognition, prevention and management of ADR.

Thus, change behavior (attitude) is not possible without the core competences about pharmacovigilance. These should be taught at undergraduate level, which should also provide practice scenarios, for example, during the internships, which enable student interaction with health professionals, companies, patients and risk mitigation strategies.

Therefore, according to Reumerman et al.[2], it is necessary to improve and innovate the teaching method of pharmacovigilance in the curricula of health courses. Rocca et al.[14] argue that a transdisciplinary approach to this practice should be promoted, which requires changes in medical education, scientific research and pharmaceutical industries.

People working in public health or other fields related to drug safety, and who are responsible for teaching and who feel a need for widespread and in-depth education in this area, will often be unsure about the topics that should most importantly be covered by pharmacovigilance[19].

Therefore, members of pharmacovigilance committees associated with the World Health Organization (WHO) or work at its collaborating centres, as well as members of the Executive Committee of the International Society of Pharmacovigilance (ISoP) or its Education and Training Project (ETP) group, or work in instit a group of WHO experts, members of the Executive Committee of the International Society of Pharmacovigilance (ISoP) or its Education and Training Project (ETP) group have proposed a curriculum for the development of minimum pharmacovigilance competences[19].

The curriculum is divided into 15 chapters, which include active teaching methodologies, hands-on exercises, and current topics such as pharmacogenetics[19]. Clinical aspects may be summarized in five key aspects (importance of pharmacovigilance, identification, management, prevention and reporting)[20], which can be integrated with other disciplines such as pharmacology and pharmacotherapy or can be taught as an independent subject[20]. The objective is to develop proactivity in pharmacovigilance activities so that predict the risk and prevent drug-induced harm, as well as produce reports with enough information that enable signal generation and causality analysis.

Nowadays, pharmacovigilance content is transmitted through lectures, with little difference regarding the workload in universities with health courses: 4 hours for medical students (mode 2h), 5.5 hours for pharmacy students and 3 hours (mode 2h) for other undergraduates[12]. The workload devoted to practice is scarce and it is exposed without student interaction and participation. This may be an independent factor that hindering academic training regarding drug safety assessment.

Thus, the curriculum proposal can be used as a model to improve the discussion of risk/benefit ratio and damage related to health technologies, especially drug treatments. In addition to the clinical domain (knowledge, understanding and experience of the effects of medications on daily health care practice), the evaluation of emerging evidences from large populations exposed to pharmacotherapy[21] is critical for good pharmacovigilance practices. Thus, evidence-based medicine and pharmacoepidemiology also should be addressed.

In this setting, current pharmacovigilance teaching in undergraduate health courses is insufficient to develop pharmacovigilance core competences. Recycling and updating the curriculum will contribute health professionals to achieve the primary goal of drug safety assessment, which is the generation of signals, that is, a hypothesis that harm has been attributed to drug use. This hypothesis will be tested in epidemiological studies.

Thus, it is possible to train professionals able to contribute for safe and rational use of medicines, improve patient safety, develop risk management protocols and evaluate the risk / benefit of the process of drug use in populations, as well as the incorporation and maintenance of new technologies in the market.

Conflicts of interest: The authors declare that they have no conflict of interest.

BIBLIOGRAPHY

1. World Health Organization, the Uppsala Centre for International Drug Monitoring. The importance of pharmacovigilance: safety monitoring of medicinal products. Geneva: World Health Organization; 2002.
2. Reumerman M, Tichelaar J, Piersma B, Richir MC, van Agtmael MA. Urgent need to modernize pharmacovigilance education in healthcare curricula: review of the literature. European Journal of Clinical Pharmacology. (2018)74:1235-1248.
3. Edwards IR. Causality assessment in pharmacovigilance: still a challenge. Drug Saf. 2017;40:365-372.
4. World Alliance for Patient Safety. who draft guidelines for adverse event reporting and learning systems: from information to action. Geneva: World Health Organization; 2005.
5. Rochon PA, Gurwitz JH. Drug therapy. Lancet. 1995;346:32-36.
6. Rochon PA, Gurwitz JH. The prescribing cascade revisited. Lancet. 2017; 389(10081):1778-1780.
7. McCarthy LM, Visentin JD, Rochon PA. Assessing the Scope and Appropriateness of Prescribing Cascades. J Am Geriatr Soc. 2019;67(5):1023-1026.
8. Cahir C, Fahey T, Teeling M, Teljeur C, Feely J, Bennett K. Potentially inappropriate prescribing and cost outcomes for older people: a national population study. Br J Clin Pharmacol. 2010;69(5):543-552.
9. DeRhodes KH. The Dangers of Ignoring the Beers Criteria-The Prescribing Cascade. JAMA Intern Med. 2019;179(7):863-864.
10. Oscanoa TJ, Lizaraso F, Carvajal A. Hospital admissions due to adverse drug reactions in the elderly. A meta-analysis. Eur J Clin Pharmacol. 2017;73(6):759-770.
11. Varallo FR, Capucho HC, Silva Planeta C, Carvalho Mastroianni PC. Possible adverse drug events leading to hospital admission in a Brazilian teaching hospital. Clinics (Sao Paulo). 2014;69(3):163-7.
12. Hartman J, Härmark L, van Puijenbroek E. A global view of undergraduate education in pharmacovigilance. Eur J Clin Pharmacol. 2017;73:891-899.
13. Melgarejo CRV, Mastroianni PC, Varallo FR. Promoção da cultura de notificação de incidentes em Saúde. São Paulo: Editora Unesp; 2019.
14. Rocca E, Copeland S, Edwards R. Pharmacovigilance as scientific discovery: an argument for transdisciplinarity. Drug Safety 2019, in press.
15. Varallo FR, Guimarães SO, Abjaude SA, Mastroianni PC. Causes for the underreporting of adverse drug events by health professionals: a systematic review. Rev Esc Enferm USP. 2014;48(4):739-47.
16. World Health Organization (WHO). Medication Without Harm - Global Patient Safety Challenge on Medication Safety. Genebra: WHO, 2017.
17. Gonzalez-Gonzalez C, Lopez-Gonzalez E, Herdeiro MT, Figueiras A. Strategies to improve adverse drug reaction reporting: a critical and systematic review. Drug Saf. 2013;36(5):317-28.
18. Varallo FR, Planeta CS, Mastroianni PC. Effectiveness of pharmacovigilance: multifaceted educational intervention related to the knowledge, skillsand attitudes of multidisciplinary hospital staff. Clinics. 2017;72(1):51-57.
19. Beckmann J, Hagemann U, Bahri P, Bate A, Boyd IW, Dal Pan GJ, Edwards BD, Edwards IR, Hartigan-Go K, Lindquist M, McEwen J, Moride Y, Olsson S, Pal SN, Soulaymani-Bencheikh R, Tuccori M, Vaca CP, Wong IC. Teaching pharmacovigilance: the WHO-ISoP core elements of a comprehensive modular curriculum. Drug Saf. 2014;37(10):743-59.
20. van Eekeren R, Rolfes L, Koster AS, Magro L, Parthasarathi G, Al Ramimmy H, Schutte T, Tanaka D, van Puijenbroek E, Härmark L. What Future Healthcare Professionals Need to Know About Pharmacovigilance: Introduction of the WHO PV Core Curriculum for University Teaching with Focus on Clinical Aspects. Drug Saf. 2018;41(11):1003-1011.
21. Andrews EB, Moore N. Man s pharmacovigilance. Oxford: John Wiley & Sons; 2014.