Original Research

Confounding Variables and the Performance of Triggers in Detecting Unreported Adverse Drug Reactions

Fabiana Rossi Varallo, PhD[1,5]; Carolina Dagli-Hernandez[2]; Caroline Pagotto[1]; Tales Rubens de Nadai, PhD[3]; Maria Teresa Herdeiro, PhD[4]; and Patricia de Carvalho Mastroianni, PhD[1]

[1]School of Pharmaceutical Sciences, UNESP-Univ Estadual Paulista, Araraquara, Department of Drugs and Medicines, Araraquara SP, Brazil; [2]School of Pharmaceutical Sciences, USP–University of São Paulo, São Paulo, Brazil; [3]Americo Brasiliense State Hospital, Department of Surgery and Anatomy, Ribeirão Preto School of Medicine, University of São Paulo, São Paulo, Brazil; [4]University of Aveiro, Department of Medical Sciences & Institute for Biomedicine–iBiMED, Aveiro, Portugal; and [5]CAPES Foundation, Ministry of Education of Brazil, Brasília – DF 70040-020, Brazil

ABSTRACT

Purpose: This study explored the performance of trigger in detecting adverse drug reactions (ADRs), the confounding variables impairing the causal association of the ADRs, and the underreporting rate by hospital health professionals.

Methods: A 6-month cross-sectional study was conducted in a public general hospital. Data collection was conducted in 2 stages: (1) screening of patient hospitalizations to identify suspected ADRs with 9 triggers developed by the Institute of Healthcare Improvement; and (2) chart review to perform the causality assessment of the suspected ADRs identified, to describe the confounding variables associated with detection of suspected ADRs that were not drug induced, and to analyze the positive predictive value of triggers in recognizing ADRs. To estimate the underreporting rate, ADRs detected by using the tool were compared with ADRs reported by health professionals during the same period.

Findings: During the study period, 3318 hospitalizations were analyzed. A total of 837 suspected ADRs were identified. However, after causality assessment, 356 were definite ADRs. Confounding variables associated with the detection-suspected ADRs were related to the clinical conditions of inpatients. The use of triggers contributed to increased ADR detection by 10.5%. The performance ranged from 0.00 to 0.75, with an overall positive predictive value of 0.43. Six ADRs were spontaneously reported, of which just 1 was also detected by using the trigger tool. Only 1 of 356 potential ADRs was reported by health professionals.

Implications: Findings show that the use of triggers contributes to detecting ADRs underreported by health professionals. However, confounding variables impaired the performance of the tool because they underestimated the causal association. Furthermore, both methods are complementary to early recognition of drug-induced harm and should be applied together in health institutions to contribute to policies of risk management, drug safety, and

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INTRODUCTION

A systematic review found that only 6% of adverse drug reactions (ADRs) are spontaneously reported.[1] This rate is a small percentage of the harm experienced by patients and is not representative of the total possibilities of occurrence of drug-induced harm.[2] Spontaneous reporting depends on the motivation of the reporters[3]; however, poor information[4–6] and the presence of confounding variables[7] also hinder causality assessment. Thus, risk communication related to drug use is ineffective.[8]

Several strategies have been developed to improve the detection of medication-related harm.[3,9–11] One approach, the use of triggers, has shown promise in improving the identification of drug safety problems. Classen et al[12] noted that the use of the tool increased ADR detection by 10-fold. However, varying performances have been observed,[13–19] as well as poor sensitivity, compared with case note review for the identification of preventable ADRs.[17]

The wide range of performance is not directly related to safety barriers, but it is instead due to the characteristics of hospitals,[15] the design and aims of studies, the sample enrolled, settings,[18] and the presence of confounding variables. Confounding occurs when the estimate of association between drug exposure and health status is distorted by the effect of one or several other variables that are also risk factors for the outcome of interest.[20] Because confounding variables are a source of bias,[21] it is critical to consider confounding variables when designing, analyzing, and interpreting studies intended to estimate causal effects. Confounding variables associated with poor performance of triggers are still unknown.

The intent of the present study was to explore and describe the relevant confounding variables, aiming to optimize the risk management of drugs in hospitals, as well as to improve safety care. Therefore, the objective of this study was as follows: to explore the performance of trigger tools in ADR; to identify the confounding variables associated with the detection of suspected ADRs that were not drug induced; and to estimate the underreporting rate by hospital health professionals.

PATIENTS AND METHODS

Study Design, Setting, and Population

A cross-sectional study was performed in a medium-complexity public, nonteaching hospital; the hospital has 30 clinical and surgical specialties and 94 beds. The study was conducted over a period of 6 months. The institution has an electronic charts system (prescription, clinical outcomes, and laboratory parameters), in which all health professionals register their assessments. In 2012, a risk management policy was implemented, including an institutional program of pharmacovigilance.

Inclusion criteria comprised all inpatients aged ≥ 18 years who had been hospitalized from November 2011 to January 2012 and from May to July 2012. The exclusion criteria included inpatients whose charts were incomplete or unavailable for consultation.

Variables

The primary outcome was the sensitivity of each trigger for ADRs. This study aimed to evaluate the association between the ADRs identified according to the trigger tool and the demographic characteristics of the inpatients enrolled (age and sex); ADR causality assessment; seriousness of ADRs; and the presence of confounding variables related to the activation of triggers.

The number of definite ADRs detected by using the trigger tool was compared with the number of ADRs reported by health professionals to estimate the percentage of improvement in safety reporting.

Data Sources/Measurement

Data were extracted from a local electronic system. Nine triggers from the list developed by the Institute of Healthcare Improvement were applied to perform the active search of ADRs (Figure).[11] Only 1 trigger ("rising serum creatinine") was adapted (to "serum creatinine >1.2 mg/dL").

Data collection occurred in 2 stages (Figure) and was performed with the aid of an instrument developed to guide the ADR evaluation process. The instrument had 5 sections with the following information: (1) reference ranges of laboratory parameters; (2) drugs associated with changes in