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CLINICAL EMERGENCY TREATMENT OF 47 CRITICAL PATIENTS WITH SEVERE POISONING AT THE HOSPITALS IN THE COUNTRYSIDE OF BRAZIL

Natalia Mucare[1], Gabriel Rodrigues Vieira[1], Gustavo Luis Contado Alves[1], Pedro Henrique Bolzani Morello[1], Paula Brandão Rodrigues Ravazzi[1],Fabiola Silva Garcia Praça[2] & Wanessa Silva Garcia Medina[*1]

[*1]Faculdades Integradas Padre Albino – FIPA, Rua dos Estudantes, 255, 15809-144, Catanduva, SP, Brazil;
[2]Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Av. do Café, s/n, 14040–903, Ribeirão Preto, SP, Brazil

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Abstract

Introduction: There are no published studies on adverse drug reactions (ADRs) as a cause of inpatient treatment for Brazilian patients. Although the Dose-Time Sensitivity Classification System has been shown to be useful for assessing ADRs in hospitalized patients. Objective: We analyzed the cases of hospitalization due to drug poisoning attending the hospitals. Methods: Standardized cases reports of 47 patients undergoing clinical therapy in hospital Padre Albino and Emilio Carlos from 2010 to 2015 were used as data collection tool to support this investigation. Results: A total 47 patients were admitted to the hospitals for exogenous intoxication, 81%, of these patients, had at least one ADR as the cause of hospital admission, with a total of a single drug reaction. The mean age of patients who experienced ADRs was about 42.31 years, among patients with ADRs, 39% were female, (47.13years), and male (39.17years). None of the women were pregnant. Conclusions: We found that the patients took between 1 and 6 medicatins and the reason for hospitalization of these patients in the countryside of the Brazil was the ADRs incidence. Our results is in the agreement with previously reported by other coutries.

Introduction

Adverse drug reactions (ADRs) are defined by the World Health Organization as a harmful and unintended response to "doses normally used in humans for prophylaxis, diagnosis or therapy of disease, or for modification of physiological function" [1].

ADRs represent a public health problem, since they account for 5-10% of hospitalizations [2,3] and also increase the length of stay [1]. In some countries, ADRs are ranked fourth to sixth leading causes of death [4-6]. In addition, they have economic repercussions; Segura and Maldonado estimated that, in 2010, they cost about 55 billion dollars (USD) in Colombia [7].

Over 30% of ADRs are potentially preventable if the role of the drug is detected at each step of the medication process [8]. However, Ferner and Aronson reported that previous estimates of the extent to which they are preventable are likely to be misleading [9]. For this reason, they proposed the dose-time susceptibility (SD-T) and EIDOS methods as prospective preventive strategies and as tools to determine retrospectively whether an adverse effect on an individual could have been prevented [10].

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There have been few studies on ADRs as the causes of admission to Intensive Care Units (ICUs) in the last 30 years. Among these, Trunet et al. [11] concluded, in 1980, that 12.6% of ICU admissions were related to iatrogenic causes, including ADRs. A retrospective 1-year study by Darchy et al. in an ICU in France aimed to determine the rate of admission to ICUs because of iatrogenic diseases. The results were compared with previous data recorded in 1979 (admission rate: 12.6%, mortality: 20%, avoidable events: 47%). They found that, in 1994, 68 (10.9%) of 623 patients were admitted to the ICU because of iatrogenic diseases and 41 cases (6.6%) were drug related. In addition, the number of prescribed drugs was considered a risk factor for iatrogenic diseases [12].

In a multicenter study by Lehmann et al., 66 (1.2%) patients were identified as having an iatrogenic medical event as the main reason for admission to the ICU. Twenty-two (34%) cases were preventable. Most of the events were secondary to technical errors (45%) or were drug related (33%) [13]. Another study looked at admissions to intensive care units prospectively for six weeks. Seventy-six of the 280 patients (27%) experienced 104 iatrogenic events, 17% of them were classified as drug-related [14].

A systematic review conducted by Vlayen et al. showed that 27 studies found that the percentage of surgical and medical adverse events requiring admission to the ICU, including drug-related events, ranged from 1.1% to 37.2% [15]. In Brazil, there were no published studies on the importance of ADRs in inducing ICU admissions. We conducted this study according to the SD-T classification for ADRs proposed by Aronson and Ferner [16] in 2003 and we noted the fact that patients had emergency admissions in most cases and that their admissions may have been due to a major health problem (for which hospitalization and close monitoring were required) that could have been related to the drug.

Materials and methods

We reviewed the patient records in the Padre Albino and Emilio Carlos hospitals from 2010 to 2015; The objective was to identify patients who were taking one or more drugs at the time of the admission, whose hospitalization was considered to be related to the drug and who were admitted to the Padre Albino and Emilio Carlos hospitals, in Catanduva, in the countryside of São Paulo, also from 19 cities in the area. All patients were admitted to the hospital.

Medical records were reviewed and evaluations were performed without any intervention or modification of the therapies. This study had the approval of the Research Ethics Committee of the Integrated Colleges Padre Albino (# 1.587.844). The causality imputation was based on previous probabilities. Statistical methods included descriptions of categorical variables through percentages and descriptions of continuous variables by trend and central dispersion measurements using 95% confidence intervals. The analyses were performed according to the observed distribution, which was verified by using the Shapiro-Wilk test.

Results

During the analysis period, 47 patients were admitted to the hospitals for exogenous intoxication, all of them were evaluated. 38 of these 47patients, had at least one ADR as the cause of hospital admission (81.25%, 95% CI 68.06% - 89.81%), with a total of a single drug reaction, since some patients presented more than an ADR (between one and three reactions). The mean age of patients who experienced ADRs was 42.31 years (range of 2 to 83 years) and 17.94% were over 60 years. Among patients with ADRs, 39.47% were female, with a mean age of 47.13 years, and 60.52% were male, with a mean age of 39.17 years. None of the women were pregnant.

Participants took between 1 and 6 medications. The causality of ADRs was classified as follows: possible in 9 cases (23.68%), probable in 28 cases (73.68%) and definitive in one case (2.63%), which was related to hydrochlorothiazide. There were no therapeutic failures in our sample and four of the cases (10.52%) were secondary to drug withdrawal.

When classifying ADRs according to the six types proposed by Edwards and Aronson in 2000, our entire sample was classified as category A. We classified them as type A when they fulfilled the following criteria proposed by Edwards and Aronson: they were common, related to an exaggerated pharmacological action of the drug (depending

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on the dose used), predictable and potentially associated with low lethality [19]. Specific cases included blood dyscrasias with predominant immunological component: neutropenia and thrombocytopenia with clindamycin and thrombocytopenia with valproic acid.

In relation to the DoTS criteria, the following distribution was established: side reactions, 0, hypersensitivity reactions, 0%, 38 of toxic reactions, 80.85%. In 10 of the cases (26.31%), age was considered a great susceptibility factor. Comorbidities (e.g. renal failure, hypoalbuminemia) influenced the occurrence of ADR in 24 cases (63.15%) and exogenous factors (eg drug interactions) in 11 cases (28.94%). In 3 cases (7.89%), a susceptibility factor could not be identified. In table 3, all of the adverse reactions are summarized according to the avoidability criteria of Schumock and Thornton. In total, 80.85% of the evaluable RADs were classified as avoidable. More than a half of the ADRs occurred due to insufficient monitoring.

Discussion

The frequency of ADRs suspected in our study was 80.85%, and these results provided the first evidence on the frequency of ADRs as a cause of hospital admission among the population ofCatanduva its region. This value is within the range established in the literature, which is approximately 1 to 37% [11-15]. In relation to other studies in Latin America, a study by Giachetto et al. [20], who evaluated ADRs causing hospitalizations or requiring withdrawal of drugs at a hospital in Uruguay, reported an admission frequency of 4.2%, which was lower than the rate in our study.

The analysis underscored the difficulty of using the Naranjo algorithm - almost all outputs were "possible" or "probable", which corresponds to the inputs that led to the initial presumptive diagnosis of ADR. The mean age of patients (71.46 years) was close to that reported in the literature, and ADRs were related to different factors in this demographic segment, including functional reserve reduction, pharmacodynamic changes and pharmacokinetics, comorbidities, polypharmacy, cognitive decline, problems social and functional limitations [21].

The most frequent ADR was cardiac arrhythmias and the affected patients had a higher average age than the rest of the evaluated population. Similarly, Marcum et al. [22] conducted a retrospective cohort study of the elderly and found that bradyarrhythmias were the leading cause of hospitalizations after ADRs, as in our study.

Electrolyte disturbances such as hyperkalemia, hyponatremia, hypokalemia and hypocalcemia were also frequent and were more common if considered as a whole. Acetylsalicylic acid (ASA) was associated with the highest frequency of 7.89% ADRs, considering a denominator of the number of them. Salvi et al. [23] reported that ADRs related to antiplatelet drugs, including clopidogrel and ticlopidine, accounted for 0% of hospitalizations. Losartan was the second most common drug associated with ADRs. This is similar to the results of a study by Pedrós [24] who found that renin-angiotensin-aldosterone blockers were more commonly associated with ADRs. However, in this study, they were linked to acute renal failure.

A bivariate analysis showed that patients with ADRs who were taking 4 or more medications had higher scores according to the Naranjo algorithm. The use of a larger number of drugs can affect the score, since one of the drugs may actually be the cause of the response. We also evaluated ADRs using the SD-T system and no side reactions were identified, i.e. none occurring within the therapeutic dosage range, all of the identified reactions were toxic reactions (i.e. at supra-therapeutic doses). This finding is not similar to the results reported by Calderón-Ospina and Bustamante in Colombian hospitalized patients [25]. However, unlike this study, most ADRs in this study were considered independent of time (80.85%). Susceptibility factors such as age, comorbidities and exogenous factors in this study differed in frequency from the aforementioned study. These findings suggest that the factors predisposing outpatients to severe ADRs may not be the same as those predisposing hospitalized patients to ADRs.

ADRs that were considered avoidable according to the Schumock and Thornton criteria constituted 44% of the cases. This figure is comparable to the results of a meta-analysis by Hakkarainen et al. [26], who found that preventable RADs occurred in 52% of cases.

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As side-effects occur at therapeutic doses, they are generally considered non-avoidable. These types of reactions represented 0% of the RADs in our study, while 80.85% were considered avoidable. This discrepancy may be explained by the fact that many reactions were considered avoidable according to criteria other than the use of a supra-therapeutic dose, e.g. the drugs were not appropriate for the patient's clinical condition, and therapeutic monitoring was not sufficiently implemented.

Regarding the limitations of this study, it was retrospective in nature and based on medical records. As we explore the occurrence of ADRs in only two hospitals, the results cannot be generalized to other settings, such as the Intensive Care Unit.

Conclusion

ADRs are a frequent cause of admissions to hospitals and can be evaluated using different assessment systems. A significant number of ADRs are preventable. National studies are necessary to assess their incidence and establish classification standards to reduce their impact. In addition, it is important to create pharmacovigilance programs for the elderly and for patients exposed to polypharmacy.

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Author Bibliography

AthorWanessa Silva Garcia Medina
Graduated in Biomedicine (1999), Master's and PhD in Toxicology from the University of São Paulo (2003 and 2008), Post-Doctorate at FCFRP-USP, Department of Pharmaceutical Sciences (2011 and 2014). Professor at the University Center Padre Albino. Coordinator of the Specialization Course in Aesthetic Health at UNIT. Member of the American Association of Pharmaceutical Scientists , President of the Student Chapter São Paulo - Brazil 2009 to 2011, Advisory Director in Aesthetic Biomedicine of National Institute of Biomedicine and member of Brazilian Association of Pharmaceutical Sciences. Scientific Initiation of FIPA supervisor, and Student Chapter FIPA Advisour, since 2014.