Prevalence of hospital admission due to adverse drug reaction in Salvador, Bahia

Antonio Carlos Beisl Noblat[1], Lúcia Araújo Costa Beisl Noblat[2], Leonardo Augusto Kister de Toledo[3], Pablo de Moura Santos[4], Márcio Galvão Guimarães de Oliveira[5], Gustavo Mustafá Tanajura[6], Silviana Ultchak Spinola[7], José Ricardo Madureira de Almeida[8]

[1] PhD in Intern Medicine from Universidade Federal da Bahia - UFBA; Relief Director of the Complexo Hospitalar Universitário Professor Edgard Santos da UFBA; and Risk Manager and Coordinator of the Centro de Farmacovigilância do Complexo HUPES, Salvador, BA
[2] PhD in Medicine and Health from UFBA; Associate Professor of Faculdade de Farmácia da UFBA; Director of Teaching, Research, and Extension of the Complexo Hospitalar Universitário Professor Edgard Santos da UFBA, Salvador, BA
[3] Specialist in Pharmaceutical Pelief from UFBA; Hospital Pharmacist; Substitute Professor of Faculdade de Farmácia da UFBA; Manager of Pharmaceutical Supply of Complexo Hospitalar Universitário Professor Edgard Santos da UFBA, Salvador, BA
[4] M.Sc. in Medicine and Health from UFBA; Hospital Pharmacist; Coordinator of the Pharmaceutical Relief Service of Complexo Hospitalar Universitário Professor Edgard Santos da UFBA, Salvador, BA
[5] Master's Degree in Medicine and Health from UFBA; Assistant Professor of Faculdade de Farmácia, Instituto Multidisciplinar de Saúde, UFBA, Salvador, BA
[6] Specialist in Hospital Infection Control and Epidemiology; Risk Manager and Coordinator of the Hospital Infection Control Service of Obras Sociais Irmã Dulce, Salvador, BA
[7] Infectologist; Coordinator of CCIH –HSR and Risk Manager, Salvador, BA
[8] Medical Director of Hospital Santa Isabel da Santa Casa da Misericórdia da Bahia, Salvador, BA

Abstract

Objective: To determine the prevalence of hospital admissions for adverse drug reaction (ADR) in Salvador, Bahia, and their outcome. **Methods:** All patients admitted to the four Sentinel Hospitals of Anvisa in Salvador, Ba, from April to December 2007 were evaluated and followed-up to determine the prevalence of admissions due to ADR and their outcomes. Cases were validated by three algorithms. The drugs were classified by the Anatomical-Therapeutic-Chemical Classification, organs and systems affected according to WHO criteria, and severity according to Pearson et al. Type of ADR was analyzed according to Rawlins and Thompson criteria.**Results:** The prevalence of ADR admissions was 0.56% and the prevalence adjusted (exposed) was 2.1%, with 316 cases. Mean hospitalization time due to ADR was 12.3 days. Young and elderly patients accounted for 28.8% and 31.1%, respectively. Females and blacks corresponded to 60% of cases. The main pharmacologic groups involved were antineoplastics, antibiotics, and diuretics, affecting skin, gastrointestinal, and hematologic systems. Approximately 70% of ADRs were validated as defined. Eighty per cent of the cases were ADR type A; recovery was observed in 90% of cases, and only one death was observed. **Conclusion:** The prevalence of ADR admission was similar to those described in literature, and only one patient died. As this is the first national study, it will serve as the basis for future investigations.

Keywords: Adverse drug reaction reporting systems; pharmacoepidemiology; hospitalization; prevalence.

Received from the Centro de Farmacovigilância, Complexo Hospitalar Universitário Professor Edgard Santos, Universidade Federal da Bahia, Salvador, BA

Submitted on: 07/08/2010
Approved on: 11/04/2010

Financial Support:
Agência Nacional de Vigilância Sanitária (Anvisa) EDITAL 01.2005

Corresponding author:
Antonio Carlos Beisl Noblat
Rua Augusto Vianna s/nº
Canela
Salvador – BA, Brazil
CEP: 40110-060
noblatufba@gmail.com

Conflict of interest: None.

Introduction

In general, hospital admissions due to adverse drug reactions (ADRs) have been a constant source of concern for health policy makers. Adverse drug reactions may be responsible for deaths and a significant increase in health costs due to prolonged hospitalizations[1,2].

The first study describing the frequency of hospitalization due to ADRs was conducted in two Belfast hospitals between 1965 and 1966, with a hospitalization frequency due to ADRs of 2.9% (37/1,268)[3]. In a university hospital in Chile, between March 1972 and March 1976, a frequency of 2.7% (53/1,958) of hospitalizations due to ADRs and 0.1% of deaths was observed[4]. In two general hospitals in the United Kingdom, between November 2001 and April 2002, a prevalence of 6.5% (1,125/18,820) of ADR hospitalizations was observed[5]. In Brazil, in 1999, in an internal medicine ward of a university hospital in Campinas, a prevalence of 6.6% (9/135) was observed[6]. The scarcity of national studies on hospitalizations due to ADRs and the lack of knowledge regarding morbidity and mortality profiles related to these reactions, along with the availability and indiscriminate use of drugs highlight the need for more studies that will contribute for planning and formulation of public health policies in this field[3]. The objective of the present study was to determine the prevalence of hospitalizations due to ADRs and their outcome in hospitals in Salvador, Bahia, Brazil.

Methods

An observational prospective study was conducted from April to December 2007 in four teaching hospitals that compose the Rede de Hospitais Sentinela da Agência Nacional de Vigilância Sanitária (Anvisa), in Salvador, Bahia, Brazil, to determine the prevalence of hospitalizations due to ADRs. Two of these hospitals are public and two are philanthropic, and they are all reference hospitals for the Brazilian Unified Health System in the state — Sistema Único de Saúde (SUS). Patients who were hospitalized for an ADR were followed-up until discharge from hospital to analyze morbidity and mortality rates, length of hospitalization, and ADR-related sequelae.

In weekly meetings, all ADR-related hospitalizations were reviewed by a group of pharmacovigilance specialists to validate the causality by applying the Naranjo[7], WHO[8], and European Union[8] Algorithms. Drugs responsible for ADRs were classified according to the Anatomical-Therapeutic-Chemical Classification Index (ATC, 1997)[9]. Affected organs and systems were classified by WHO criteria, the WHOART[10]. Type of reaction was analyzed by Rawlins and Thompson criteria (1991)[11].

Data on hospitalized patients due to ADRs were recorded in a databank and reviewed using the SPSS for Windows version 10.0 software[12]. Descriptive simple frequency analysis was used to determine the even prevalence, drugs and reactions more commonly involved, as well as their outcome. For analysis of overall prevalence, cases of ADR hospitalizations represented the numerator and the total number of admission the denominator. Adjusted prevalence was calculated based on patients exposed, i.e., those whose cause of hospitalization was not elective surgeries.

The determination of length of hospitalization for ADRs in the aforementioned hospitals was done by calculating the mean.

This study was approved by the Ethics Committees of the four hospitals in the Rede Sentinela. Patients were only included in the study after they, or their legal representative, signed the informed consent. Patient identification data was kept confidential.

Results

The characteristics of patients hospitalized for ADRs and pharmacologic group involved are shown in Table 1.

Total prevalence of ADRs was 0.56% (212/37,658); adjusted prevalence was 2.1% (212/10,276); the 212 patients hospitalized had a total of 316 reactions. Mean length of hospitalization was 12.3 ± 12.7 (1-77) days (2,490/202), with median of 8 days. A mean of 4,184 patients was hospitalized, although the denominator of exposed individuals was 10276 patients due to the high frequency of patients admitted for elective surgeries, approximately 73% (10,276/37,658). Main organs and systems affected included: hematologic system, 32.6% (103/316); skin, 18.7% (59/316); gastrointestinal system, 14.6% (46/316); liver and gallbladder, 7% (22/316);

Table 1 – Characteristics of patients hospitalized for ADRs and pharmacologic group involved, April to December 2007, Salvador, BA, Brazil

Variable	n/N (%)
Gender	
Male	85/212 (40)
Female	127/212 (60)
Race	
Caucasian	83/212 (40.5)
Black	129/212 (59.5)
Age group	
0 to 19 years	61/212 (28.8)
20 to 39 years	33/212 (15.6)
40 to 59 years	52/212 (24.5)
Equal or greater than 60 years	66/212 (31.1)
Pharmacologic groups	
Antineoplastics	146/361 (40.4)
Antibiotics	28/361 (7.8)
Diuretics	26/361 (7.2)
Non-opioid analgesics	25/361 (6.9)
Antithrombotics	22/361 (6.1)
Steroid anti-inflammatories	18/361 (5)
Antimycobacterial	16/361 (4.4)
Non-steroidal anti-inflammatories	14/361 (3.9)
Others	66/361 (18.3)

central and peripheral nervous system, 5.7% (18/316); general status, 5.1% (16/316); urinary system, 4.1% (13/316); cardiovascular system, 3.5% (11/316); endocrine system, 2.8% (9/316); metabolism and nutrition, 2.2% (7/316); respiratory system, 0.9% (3/316); eyes, skeletal musculature, and extra-cardiac vascular system, 0.6% (2/316); and other, 0.9% (3/316). The main reactions presented by patients included: pancytopenia, 9.2% (29/316); fever, 4.1% (13/316); thrombocytopenia, 4.1% (13/316); vomiting, 4.1% (13/316); skin rash, 3.8% (12/316); neutropenia, 3.8% (12/316); anemia, 3.5% (11/316); and pruritus, 3.5% (11/316). Using methods to analyze the causality relationship, approximately 70% of ADRs were classified as certain or proven. Regarding type, 80% (252/316) of cases were classified as A. Table 2 describes the main outcomes.

Table 2 – Outcomes of patients hospitalized for ADRs, April to December 2007, Salvador, Bahia, Brazil

Variable	n/N (%)
Type	
Recovery	192/212 (90.6)
Death from other causes	13/212 (6.1)
Unknown	6/212 (2.8)
Fatal	1/212 (0.5)
Sequela	
Yes	12/212 (5.7)
No	200/212 (94.3)

Discussion

The prevalence of ADRs seen in this study was similar to that of international studies[1-6]. Literature data demonstrate a wide variation in hospitalization frequency due to ADRs[13,14]. This can be explained by factors like the diversity of methodologies used in different studies and methods for detection of ADRs at the time of hospital admission, as well as establishing a cause, in addition to population and hospital characteristics. Other possible explanations include the lack of culture of notification of ADRs, lack of diagnosis of ADR in the hospitalization request form, and also the fact that ADRs are not always listed as a health problem.

The prevalence of hospitalization for ADRs in blacks was expected, as the population of Salvador is predominantly black (82.9%) (IBGE, 2009)[15]. On the other hand, the high prevalence of hospitalization for ADRs in Caucasians can be explained by the admission profile in the two philanthropic hospitals. Females were more prevalent, as they seek health care services more often than males[16], and, therefore, they use more medications and are more prone to develop adverse reactions.

The age groups more often affected were similar to those reported in other studies, reinforcing young and elderly patients as risk groups for ADRs[17]. One of the explanations for this is the existence of physiological conditions that determine pharmacokinetic and pharmacodynamic changes in these age groups[18].

As for the main pharmacological group (antineoplastics), it reflects both characteristics of the institutions and profiles of patients seen in these Reference Services. Reactions to antineoplastics drugs are considered predictable but not preventable, due to their pharmacological effect, since these manifestations are the side effects of these treatments explained by exacerbation of their pharmacologic action. Additionally, antineoplastic treatment is performed in association with other drugs that can increase the risk of developing ADRs[19,20].

The main organs and systems involved in ADRs reflect the main actions of the group of drugs used more often by the population of this study. Hematologic ADRs, i.e., changes in cell counts and other blood dyscrasias, are among the main problems related to antineoplastic therapy, being one of the causes of treatment discontinuation[19,20]. Since skin lesions are more visible and, occasionally, symptomatic, they are more commonly seen in emergency services, with a significant increase in morbidity and mortality, besides increasing health care costs[21].

Most ADRs was type A, which means they are dose-dependent, with elevated morbidity and low mortality and, therefore, predictable, but not always preventable. This might explain the high recovery rate of most cases in this study. The only death observed was a case of stroke caused by warfarin use.

Casualty analysis by Naranjo, WHO, and European Union algorithms showed that most reactions were validate as certain and likely, although ADR diagnosis was confirmed in all cases. The explanation why algorithms do not demonstrate 100% certainty is due to the fact that some of the questions cannot always be applied to cases, as well as reflect Health Services deficiencies (lack of serum levels, objective laboratorial demonstration, polypharmacy, and specific patient monitoring)[22].

Conclusion

The prevalence of hospitalization for ADRs in the present study was similar to data in international literature, with only one death. Since this is the first national study with populational representation, it should be the basis for future studies.

Acknowledgments

We would like to extend our gratitude to the field investigators (Jane Meire Magalhães Carneiro, Sóstenes Mistro, Nadja Pereira de Souza, Glaúcia Beisl Noblat Cerqueira de Carvalho, Sebastião Lomba Neto, Bartya Lima de Almeida Leite, Geisa Queiroz de Almeida) for gathering data in the four Hospitals.

Special thanks to Professor Dr. John Kessler – Chairman of the Institutional Review Board – Duke University, Chapel Hill, North Carolina, USA.

To the pharmacists Rosa Martins and Ivellise Souza of the Drug Information Center of Universidade Federal da Bahia.

References

1. Olivier P, Boulbes O, Tubery M, Lauque D, Montastruc JL, Lapeyre-Mestre M. Assessing the feasibility of using an adverse drug reaction preventability scale in clinical practice: a study in a French emergency department. Drug Saf. 2002; 25:1035-44.
2. Waller P, Shaw M, Ho D, Shakir S, Ebrahim S. Hospital admissions for drug-induced disorders in England: a study using the Hospital Episodes Statistics (HES) database. Br J Clin Pharmacol. 2005; 59:213-9.
3. Hurwitz N. Admissions to hospital due to drugs. Brit Med J. 1969; 1:539-40.
4. Naranjo CA, Gonzalez G, Ruiz I, Busto U. Hospital admissions due to adverse drug reactions. Rev Med Chile. 1978; 106:192-5.
5. Pirmohamed M, James S, Meakin S *et al*. Adverse drug reactions as cause of admission to hospital: prospective analysis of18 820 patients. BMJ. 2004; 329(7456):15-9.
6. Pfaffenbach G, Carvalho OM, Bergsten-Mendes G. Drug adverse reactions leading to hospital admission. Rev Assoc Med Bras. 2002; 48:237-41.
7. Naranjo CA, Busto U, Sellers EM *et al*. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981; 30:239-43.
8. Organização Mundial da Saúde. Monitorização da segurança de medicamentos: diretrizes para criação e funcionamento de um Centro de Farmacovigilância. Brasília (DF): Organização Pan-Americana da Saúde; 2005.
9. World Health Organization. WHO Collaborating Centre for Drug Statistics Methodology. Norwegian Institute of Public Health. Anatomical-Therapeutic-Chemical Classification Index (ATC, 2006). Available from: http://www.whocc.no/atcddd/July 2006.
10. World Health Organization. Collaborating Center for International Drug Monitoring of Adverse Reaction Terminology. WHO: Uppsala; 1984.
11. Rawlins M, Thompson J. Mechanisms of adverse drug reactions. In: Davies D, editor. Textbook of adverse drug reactions. 4th ed. Oxford: Oxford University Press; 1991.
12. Norusis MJ. SPSS 10.0 Guide to Data Analysis. Englewood Cliffs: Prentice Hall; 2000.
13. Van der Hooft CS, Sturkenboom MC, van Grootheest K, Kingma HJ, Stricker BH. Adverse drug reaction-related hospitalisations: a nationwide study in The Netherlands. Drug Saf. 2006; 29:161-8.
14. Sinha U, Raha S, Wilkins E. Adverse drug reactions and hospital admission of older patients. Age Ageing. 2000;29:551-2.
15. Instituto Brasileiro de Geografia e Estatística (IBGE). Indicadores de cor ou raça, segundo a Pesquisa Mensal de Emprego. Março, 2009. [citado 7 out 2010] Disponível em: http://www.ibge.gov.br/home/estatistica/indicadores/trabalhoerendimento/pme_nova/marco2009.pdf.
16. Pinheiro RS, Viacava F, Travassos C, Brito AS. Gênero, morbidade, acesso e utilização de serviços de saúde no Brasil. Ciênc Saúde Coletiva. 2002; 7:687-707.
17. Chan M, Nicklason F, Vial JH. Adverse drug events as a cause of hospital. admission in the elderly. Intern Med J. 2001; 31:199-205.
18. Nies AS, Spielberg SP. Principles in therapeutics. In: Brunton LL, Lazo JS, Parker KL, editors. Goodman & Gilman´s. the pharmacological basis of therapeutics. New York: Mc Graw-Hill. 2006; p.43-62.
19. Cairo MS. Dose reductions and delays: limitations of myelosuppressive chemotherapy Oncology (Williston Park). 2000; 14(9 Suppl 8):21-31.
20. Kueh YK. Haematological adverse drug reactions in hospital practice. Ann Acad Med Singapore. 1991; 20:106-13.
21. Gomes ER, Demoly P. Epidemiology of hypersensitivity drug reactions. Curr Opin Allergy Clin Immunol. 2005; 5:309-16.
22. Macedo AF, Marques FB, Ribeiro CF, Teixeira F. Causality assessment of adverse drug reactions: comparasion of the results obtained from published decisional algorithms and from the evaluations of an expert painel, according to different levels of imputability. J Clin Pharm Ther. 2003; 28:137-43.