Causes of drug-related problems in the emergency room of a hospital in southern Brazil

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A B S T R A C T
Objective: To assess the frequency and types of drug-related problems (DRPs) in patients seeking emergency care in a teaching hospital in southern Brazil and to identify the possible causes and drugs involved in these problems.

Method: A cross-sectional study was performed, using a structured questionnaire for data collection. Multivariate logistic regression was used to control for possible confounding factors and to establish an independent association between the presence of DRPs and the amount of medication, patient’s age and their educational level.

Results: A total of 350 patients were interviewed. The frequency of DRPs was 31.6%. Quantitative ineffectiveness was observed in 30.9% of DRPs and the main cause of the DRP was an inadequate dosing regimen. Sixty-six DRPs (53.7%) were caused by the health system or the health professionals. Factors independently influencing the development of DRPs were educational level and the number of drugs being taken.

Conclusions: Our data suggest that one-third of the patients attending the emergency room of our hospital had a drug-related problem, highlighting the importance of considering drugs as a possible cause of health problems and the need for their more rational use.

Introduction

Although many efforts have been made to enforce the rational use of drugs, several studies have reported drug-induced health problems.1–3 The most commonly mentioned factors involved in these problems are the social pressures to which prescribers are subjected, the structure of the health system and pharmaceutical marketing.4 Patients also play an important role in this phenomenon, since they may agree to treatment and then show only partial adherence or may simply decide not to adhere to the treatment.5 The large-scale use of drugs may create situations that do not follow pharmacotherapeutical principles. These situations are classified as drug-related problems (DRPs).6 The first studies on the
The ability to prevent these events is essential. In line with the previous studies that have focussed on this issue, therapy optimization aimed at preventing DRPs improves health, reduces morbidity and increases quality of life. DRPs were identified case by case, based on the classification of the Brazilian Pharmaceutical Care Consensus. In line with the basic principles of pharmacotherapy, DRPs were classified by evaluating three distinct criteria of pharmacotherapy: indication, effectiveness and safety. Suspected adverse drug reactions (ADR) were classified according to Naranjo’s algorithm. The causality of the remaining DRPs was inferred by using data from the questionnaire and the emergency department records.

To estimate interobserver variability, 67 random cases (20%) were analyzed by a second pharmacist. No divergence in classification was found.

Patients who were classified in the polypharmaceutical category were those who had used five drugs or more concurrently for 10 days before seeking emergency care. The drugs were classified according to the Anatomical Therapeutic Chemical system. The analysis was performed using Epi Info® 6.0 and SPSS 18.0 software. A descriptive analysis using measures of central tendency and dispersion of the sample was performed. The magnitude of the associations was estimated by odds ratios (OR) with a confidence interval of 95% (CI95%). The chi-square test was used to determine statistical significance between proportions. To control for possible confounding factors and to establish an independent association between the presence of DRPs and the number of medications, age and educational level, a multivariate logistic regression analysis was performed. The model included variables with a p value of <0.20.

**Results**

**Sample characterization**

Three hundred and fifty patients were interviewed, of whom 15 were excluded due to lack of data. Consequently, the final sample was composed of 335 patients, who were predominantly female (65.7%) and white (76.7%). The mean age was 44.9 years (SD = 19.2). Most (61.4%) had elementary education and were from the metropolitan area of Porto Alegre (94.9%) (Table 1).

**Drug-related problems**

Of the 335 patients, 106 (31.6%; CI95%; 26.7–36.9) sought emergency care due to DRPs. A total of 123 DRPs were observed, representing 1.2 DRPs per patient. Exclusion of data. Consequently, the final sample was composed of 335 patients, who were predominantly female (65.7%) and white (76.7%). The mean age was 44.9 years (SD = 19.2). Most (61.4%) had elementary education and were from the metropolitan area of Porto Alegre (94.9%) (Table 1).

Calculation of the sample size was based on a previous study that estimated a DRP prevalence of 24.3% in an ER in Spain. Based on an annually-served population of 65,700 patients, a significance level of p ≤ 0.05 and variation of 5%, the estimated minimum number of individuals needed for interview was 281. This study included patients older than 12 years who were capable of expressing themselves or who were accompanied by a caregiver. Caregivers answered all questions and were present at the medical consultation. When the patient could not remember any information during the interview, the questionnaire was completed later via a telephone contact.

The review board of our institution, which is accredited by the Office of Human Research Protections as an Institutional Review Board, approved the ethical and methodological aspects of the project, and all patients signed a written informed consent form to participate in this study.

A recent study reported that around 90% of DRPs are preventable. The ability to prevent these events is essential to identify possible causes and structurally-related factors. Few published studies that have focussed on this issue. Therapy optimization aimed at preventing DRPs improves health, reduces morbidity and increases quality of life.

Published studies report DRPs as a frequent cause of visits to emergency services and hospitalization and data on this topic are scarce in developing countries. The aim of the present study was to assess the frequency and types of DRPs in patients seeking emergency care in a teaching hospital in southern Brazil and to identify the possible causes and drugs involved.

**Method**

This cross-sectional study was conducted at the ER of the Hospital de Clínicas de Porto Alegre (Brazil) for 1 month, which provides emergency care to approximately 65,700 patients annually from Porto Alegre (63.9%) and from other areas (36.1%) in southern Brazil.

A structured questionnaire was used to collect data. The development of this questionnaire has previously been published. Data collection was performed by a properly trained and validated team of interviewers in three emergency care shifts (morning, afternoon and night) every day of the week for 20 days. The interviews were carried out as illustrated in the patient care flowchart (Fig. 1) before the patient was seen by a doctor. Data on the reasons for consultation, the basic illness, hospitalization, symptoms, measurements of blood pressure and blood glucose level were collected or confirmed in the emergency department records after the physician consultation. If the patient was hospitalized, the medical records were consulted.

<table>
<thead>
<tr>
<th>Patient identification</th>
<th>Screening (Nurse)</th>
<th>Reception (Doctor’s visit scheduling)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interviews carried out</td>
<td>Medical consultation</td>
<td>Exclusion (inexistence of data)</td>
</tr>
<tr>
<td>350 patients</td>
<td>350 patients</td>
<td>15 patients</td>
</tr>
<tr>
<td>Total sample</td>
<td>335 patients</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1.** Location of the interviews carried out in the patient care flowchart.
Table 1
Patient characteristics of patients, according to the presence of drug-related problems.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No DRP (n = 229)</th>
<th>With DRP (n = 106)</th>
<th>Total (n = 335)</th>
<th>Significance p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (standard deviation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 years</td>
<td>42.9 (18.7)</td>
<td>49.3 (19.7)</td>
<td>44.9 (19.2)</td>
<td>0.030</td>
</tr>
<tr>
<td>65 years or older</td>
<td>189 (82.5)</td>
<td>76 (71.7)</td>
<td>265 (79)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>154 (67.2)</td>
<td>66 (62.3)</td>
<td>220 (65.7)</td>
<td>0.459</td>
</tr>
<tr>
<td>Male</td>
<td>75 (32.8)</td>
<td>40 (37.7)</td>
<td>115 (34.3)</td>
<td></td>
</tr>
<tr>
<td>Polypharmacy user</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to four drugs</td>
<td>192 (84)</td>
<td>70 (66)</td>
<td>262 (78)</td>
<td>0.001</td>
</tr>
<tr>
<td>Five drugs or more</td>
<td>37 (16)</td>
<td>36 (34)</td>
<td>73 (22)</td>
<td></td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No schooling</td>
<td>8 (3.5)</td>
<td>11 (10.4)</td>
<td>19 (5.7)</td>
<td></td>
</tr>
<tr>
<td>Elementary education</td>
<td>131 (57.2)</td>
<td>75 (70.8)</td>
<td>206 (61.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>High school education</td>
<td>75 (32.8)</td>
<td>12 (11.3)</td>
<td>87 (26)</td>
<td></td>
</tr>
<tr>
<td>Higher education degree</td>
<td>15 (6.5)</td>
<td>8 (7.5)</td>
<td>23 (6.9)</td>
<td></td>
</tr>
<tr>
<td>Origin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metropolitan region</td>
<td>218 (95.2)</td>
<td>100 (94.3)</td>
<td>318 (94.9)</td>
<td></td>
</tr>
<tr>
<td>Countryside</td>
<td>8 (3.5)</td>
<td>6 (5.7)</td>
<td>14 (4.2)</td>
<td>0.331</td>
</tr>
<tr>
<td>Other states</td>
<td>3 (1.3)</td>
<td>-</td>
<td>3 (0.9)</td>
<td></td>
</tr>
<tr>
<td>Skin color</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>174 (76.0)</td>
<td>83 (78.3)</td>
<td>257 (76.7)</td>
<td>0.503</td>
</tr>
<tr>
<td>Black</td>
<td>21 (9.2)</td>
<td>8 (7.5)</td>
<td>29 (8.7)</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>34 (14.8)</td>
<td>14 (13.2)</td>
<td>48 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>1 (0.9)</td>
<td>-</td>
<td>1 (0.3)</td>
<td></td>
</tr>
</tbody>
</table>

DRP: drug-related problems.

A high school educational level was a protective factor against the development of DRPs (OR = 0.32; CI95%: 0.16–0.64). The use of five or more drugs contributed independently to the occurrence of DRPs (OR = 2.21; CI95%: 1.3–3.9) (Table 2).

The most frequent DRPs were ineffectiveness and unsafe use, respectively (Table 3). Ineffectiveness was related mainly to inadequate dosage regimens (22 cases; 17.9%) and refractoriness (15 cases; 12.2%). Adverse drug reactions were the principal cause of safety problems (35 cases; 28.5%).

Factors involved in drug-related problems

In 21 DRPs (17.1%) the patient was identified as the main causative factor. The most common reasons were lack of adherence to treatment and self-medication. The drug itself was linked to 36 DRPs (29.3%). The remaining 66 DRPs (53.7%) could be attributed to the health system itself or to healthcare professionals.

Drugs most commonly involved in drug-related problems

Of the 71 drugs related to DRPs, the most frequently involved were those acting on the cardiovascular system (24.3%) and on the nervous system (18.6%). These drug groups contain agents such as captopril (reported in 11 DRPs) and lithium carbonate (reported in 6 DRPs). Over-the-counter drugs formed a group of nine drugs (12.7%), which were reported in 16 DRPs (13%).

Table 2
Variables independently associated with the presence of drug related problems.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Odds ratio</th>
<th>Confidence interval 95%</th>
<th>Significance p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;65 years</td>
<td>1</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>65 years or older</td>
<td>1.14</td>
<td>0.65–2.11</td>
<td>0.688</td>
</tr>
<tr>
<td>Polypharmacy user</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to four drugs</td>
<td>1</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Five drugs or more</td>
<td>2.21</td>
<td>1.3–3.9</td>
<td>0.005</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No schooling</td>
<td>1.93</td>
<td>0.69–5.40</td>
<td>0.210</td>
</tr>
<tr>
<td>Elementary education</td>
<td>1</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>High school education</td>
<td>0.32</td>
<td>0.16–0.64</td>
<td>0.001</td>
</tr>
<tr>
<td>Higher education degree</td>
<td>1.02</td>
<td>0.41–2.57</td>
<td>0.969</td>
</tr>
</tbody>
</table>

Discussion

In this study, the frequency of DRPs is higher than that reported by other authors, who found frequencies ranging from 24.3% to 29.0%. The number of DRPs per patient was similar to that found by Martínez-Romero et al (1.1 DRPs/patient). Our results agree with those reported in published studies that demonstrate that the number of drugs in use is related to the development of DRPs. Additionally, this study shows that patients with a high school education have a lower odds of developing DRPs than those with less schooling.

Indication-related drug-related problems

The reasons for non-adherence to the treatment prescribed were cost or probably a drug supply problem in the public system during the study period, which lowered affordability difficult and affected the treatment of these patients. Self-medication was identified in a few cases and involved over-the-counter drugs. Responsible practice of self-medication should be emphasized, both by the user and by the professional recommending the medication.

Effectiveness-related drug-related problems

The high frequency of effectiveness-related problems (54.5%) agrees with that reported by Baena et al (62.7%). Most of these DRPs involved drugs of continuous use that require monitoring by the healthcare team. In our system, continued and multiprofessional care is not always provided due to deficiencies in the public health service. Consequently, the patient may resort to seeking
According to O'Connor, treatment failure is due to 20 DRPs suspected of being ADR and, in one patient, two DRPs were suspected of being ADR, totaling 36 suspected cases. According to Naranjo's algorithm, 20 DRPs suspected of being ADR were classified as probable and 16 as possible. No DRPs suspected of being ADR were classified as definite or doubtful. Considering only the probable suspected case, we found a 6% frequency of seeking ER care due to ADRs, which is similar to the frequency range (1%-5%) reported by other authors. The clinical manifestations observed ranged from mild to severe.

Importantly, the ER medical team recorded the suspected ADRs in only 30.5% of the cases. The pharmacovigilance system in Brazil is relatively new and hence few health professionals perceive drugs as a potential cause of health problems. Additionally, there is a lack of educational measures to improve the safety of drug therapy, which may be related to the high rate of ADRs.

### Safety-related problems

Thirty-five cases (97%) of safety-related DRP were suspected of being ADR and, in one patient, two DRPs were suspected of being ADR, totaling 36 suspected cases. According to Naranjo’s algorithm, 20 DRPs suspected of being ADR were classified as probable and 16 as possible. No DRPs suspected of being ADR were classified as definite or doubtful. Considering only the probable suspected case, we found a 6% frequency of seeking ER care due to ADRs, which is similar to the frequency range (1%-5%) reported by other authors. The clinical manifestations observed ranged from mild to severe.

### Factors involved in drug-related problems

In 21 DRPs (17.1%), the patient was identified as the main causative factor. The most common reasons were lack of adherence to treatment due to neglect of one or more doses of medicines for chronic use or the decision not to continue treatment and self-medicating.

The drug itself was linked to 36 DRPs (29.3%). Access to drug information from the healthcare team could help to reduce predictable ADR. Thus, pharmacovigilance programs, structuring of drug information centers and involvement of professionals specialized in drug use in the healthcare teams should be encouraged.

The remaining 66 DRPs (53.7%) can be attributed to the health system itself or to healthcare professionals, specifically to the prescriber, since in Brazil the participation of other professionals is still low. We chose to group these cases into a single category. The study design did not allow data on previous visits to the ER to be collected for a more detailed analysis. In many cases, medical inertia was evident, but whether this was intrinsic or due to the organization of the health system is unclear.
Drugs most commonly involved in drug-related problems

Chronic patients, who take drugs every day, are expected to show a higher number of DRPs than patients who take drugs sporadically. The frequent association of drugs from these classes with DRPs has already been reported. Over-the-counter drugs should present no risk of use, but their possible use without proper instruction might have resulted in a health problem that required the ER service. This possibility may be related to the failure of the pharmacists to take responsibility for rational self-medication in Brazil.

Study limitations

One of the main limitations of this study is that it is based on reported data, leading to considerable uncertainty on the possible causes of the DRPs identified. This uncertainty was reduced by collecting information such as diagnosis and outcome of medical examinations from medical records.

Another issue is that multiple causes can be involved in DRPs and each of the factors listed as important may be underestimated, since only the most likely cause for each DRP was given. To estimate the responsibility of professionals, patients or the organization of the health system and to evaluate the contribution of each factor to the development of a specific DRP, longitudinal studies are required, as well as adjustments to the original questionnaire. Despite these limitations, we believe that the data may be useful for designing strategies to reduce the percentage of DRPs found.

Conclusion

The data obtained in our study show that a high proportion of patients sought ER care due to DRPs and that the risk of DRPs increases with the number of drugs added to the therapy. These results reinforce the importance of considering drugs as a possible cause of health problems and of the need to develop public policy strategies to make the use of this resource more rational.

Since most patients had a low educational level, better counseling on disease(s), drug(s) and self-medication risks may positively influence treatment adherence and safety. Our data suggest that patients, especially chronic patients, are receiving insufficient attention from health teams, possibly due to appointment overbooking and to a lack of training in the systematic evaluation of pharmacotherapy and counseling. The organization of the health system could help to reduce DRPs by enabling more frequent outpatient clinic visits with a multidisciplinary team and implementing a pharmacotherapeutical monitoring system. Such measures may decrease demand for more complex care, such as that provided by the ER service.

What does the study add to the literature?

A high proportion of patients sought emergency service due to drug related problems. Physician and health system were probably responsible for 53.7% of the cases, while drug and the patient were related to 29.3% and 17.0% of the problems observed, respectively. The health system organization could contribute to reduce drug related problems by enabling more frequent ambulatory visits with multidisciplinary team and the implementation of a pharmacotherapeutic monitoring method.

Authors’ contributions

R.S. Andreazza and I. Heineck conceived the study, supervised all aspects of its implementation, collected data, performed the analysis, interpreted the data and contributed to writing the first draft of the manuscript. P.S. Köche and M.S. Castro interpreted the data and contributed to writing the first draft of the manuscript. All authors contributed ideas, interpreted the data and reviewed drafts of the manuscript. All authors approved the final version. R.S. Andreazza is responsible for the article.

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Conflict of interest

None.

References


What is known about this topic?

Several studies have reported drug-induced health problems and report drug related problems as a frequent cause of visits to emergency services and hospitalization. Data on this topic are scarce in developing countries. The objective of this study was to assess the frequency and types of drug related problems in patients seeking emergency care in a teaching hospital in southern Brazil and to identify the possible causes and drugs involved.


