Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense)*
Lat. Am. J. Pharm. **30** (7): 1342-7 (2011)

Regular Article
Received: August 3, 2010
Revised version: May 5, 2011
Accepted: May 7, 2011

Development of Risk Score to Hospitalized Patients for Clinical Pharmacy Rationalization in a High Complexity Hospital

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SUMMARY. **The aim of the present research was to build a tool to classify patients according to drug theraphy risk so as to rationalize the use of clinical pharmaceutical resources in hospital settings. Risk factors selected in the literature available were carefully revised to be included in the score. The selected factors were submitted to univariate and then to multivariate analysis. The significant results were included in the final score model, which divided the hospitalized patients into three groups: low risk, moderate risk and high risk. After that, the score was applied in the hospital and a "risk classification" map was created of the various sectors of the Hospital de Clínicas de Porto Alegre. The score was applied to 1442 patients in nine different areas of the hospital, with 398 (27.6 %) of them presenting high risk, 612 (42.4 %) moderate risk and 432 (29.9 %) low risk. The high risk units were: Pediatric Oncology, the Intensive Care Unit (ICU) for adults and the Pediatric Intensive Care Unit (PICU). The clinical and surgical units, the Protected Environment Unit (PEU) and the Neonatal Intensive Care Unit (NICU) were classified as moderate risk and the pediatric hospitalization unit as low risk. Considering the patients with renal and/or hepatic problems, cardiac and/or pulmonary problems and immunosuppression and/or immuno deficiency, 50.2 %, 61.5 % and 52.6 %, respectively, presented high score, with all of them taking at least one risk drug. Regarding the number of drugs prescribed, the use of 0-5 drugs was verified in 68.8 % of the patients with low score and the use of 11-15 drugs in 63.1 % of the patients with high score. The score developed in this study showed a significant correlation between the risk groups and the profile of the patients hospitalized in the analyzed areas. This tool will be validated to optimize pharmaceutical care resources.**

INTRODUCTION

Adverse drug events (ADEs) are a public health problem, with high morbidity and mortality, accounting for 3 to 23 % of all hospitalizations [1]. In USA, ADEs are among the 4th and 6th major causes of death. The clinical protocols available recommend a large variety of drugs for clinical treatment. Consequently, many patients take innumerous drugs, a situation known as polypharmacy [2,3].

Polypharmacy is regularly considered a risk factor, used as an indicator to identify patients that require special attention. An increased number of drug intake causes the number of drug-related problems (DRP) to increase by 8.6 % [2]. The incidence of adverse events increases proportionally with the number of drugs administered. The use of 20 drugs or more increases the risk of adverse reaction by 45 % [5].

In this context, the purpose of pharmaceutical care is to offer drug-related actions and services focused on the relation with patients and the multiprofessional health team, to promote the rational use of drugs [6,7]. The pharmaceutical monitoring is a continuous process, whose purpose is to identify and solve drug-related problems, and the utilization of a standardized methodology is a basic requirement to perform interventions [8-10].

KEY WORDS: Clinical pharmacy, Rationalization hospitalized patients, Risk score.

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ISSN 0326-2383

Due to the required rationalization of pharmaceutical clinical resources in health care centers, the selection of patients is necessary, prioritizing those at higher risk of developing drug-related problems [11,12].

The Hospital de Clínicas de Porto Alegre is a highly complex tertiary hospital with 784 beds. It is linked to the Federal University of Rio Grande do Sul and it serves basically users of the National Public Health System.

The purpose of this study is to develop an instrument to assess drug-related risk factors according to the profile of hospitalized patients so as to guide the allocation of pharmaceutical care.

MATERIAL AND METHODS

Risk score elaboration

Specific methodologies were considered in the score elaboration, and those that define levels of attention in other situations were taken as examples, such as the existing scores for nursing attention and nutrition for risk screening in hospital-medical care services, as well as the main factors associated with adverse effects and drug interactions [13-15]. The score was elaborated to classify the patients as low, moderate and high risk groups (Figs. 1 and 2).

Score/sample application

In Protected Environment Units (PEU)

Patient's conditions		**Score**
Patient uses:	0 – 5 drugs	1
	6 – 10 drugs	2
	11 – 15 drugs	3
	16 drugs or more	4
Endovenous drugs:	None	0
	1 – 3	1
	4 or more	2
Patient takes potentially harmful drugs:	No	0
	Takes 1	1
	Takes 2 or more	2
The patient:	Does not use a tube	0
	Uses NET, NGT, JF, OET or GF	1
	Uses Total Parenteral Nutrition (TPN)	2
Patient's age:	0 to 14 years old	2
	15 to 65 years old	1
	> 65 years old	2
Patient has renal and/or hepatic problems:	Yes	1
	No	0
Patient has cardiac and/or pulmonary problems:	Yes	1
	No	0
Patient has immunosuppression and/or immunocommitment:	Yes	2
	No	0
TOTAL		

	Application of monitoring definition criteria
≥ 9	High risk: patients with elevated risk factors requiring monitoring priority.
5 - 8	Moderate risk: intermediate patients, requiring monitoring, but not on emergency basis.
≤ 4	Low risk: patients that should be only observed and monitored.

Figure 1. Form for risk score application. Information to be consigned: Patient's Name, Clinical Records, Bed No. and Date.

Classification of risk factors for the definition of monitoring to hospitalized patients	
Patient's conditions	**Descriptions of criteria**
Patient uses: 0–5 drugs / 6–10 drugs/ 11– 15 drugs/16 drugs or more	Calculate the number of oral (OA) and endovenous (EV) administration items (not including creams and salves). Consider all FT items, excluding Dipyrone, Paracetamol & Metoclopramide.
Endovenous drugs	Calculate the number of EV items prescribed, including NT items, excluding Dipyrone, Paracetamol & Metoclopramide.
The patient takes potentially harmful drugs	Antineoplastic drugs (all), Adenosine EV, Adrenaline EV. Amikacin EV, Amiodarone EV, Atracurium EV, Pancuronium EV, Potassium chloride EV push, Deslanoside EV, Dexamethasone EV, Diazepam EV, Dopamine EV, Dobutamine EV, Esmolol EV, Streptomycin EV, Phenytoin EV/OA, Fentanyl EV, Flumazenil EV, Gentamycin EV Heparin EV, Hydrocortisone EV, Hydroxyzine EV, Insulin EV, Lidocaine EV, Methylprednisolone sodium succinate EV, Metoprolol EV, Midazolam EV, Morphine EV, Naloxone EV, Nitroglycerine EV, Nitroprussiate EV, Noradrenaline EV, Promethazine EV, Rocuronium EV, Succinylcholine EV, Teicoplanine EV, Vancomycin EV, Warfarin OA
The patient uses enteral/gastric tube. The patient uses TPN. If tube and TPN, consider the highest use.	NET (naso-enteral tube), NGT (nasogastric tube), GF (gastrostomy feeding), JF (jejunostomy feeding), OET (oral-enteral tube). TPN (Total Parenteral Nutrition)
The patients has renal/ hepatic problems.	Acute or chronic kidney failure, liver failure and/or cirrhosis. Check medical records.
The patient has cardiac/ pulmonary problems.	COPD, mechanical ventilation (MV), cystic fibrosis, heart failure (acute or if ejection fraction ≤ 35 %, cardiogenic, septic, hypovolemic shock. Check medical records.
The patient has immunosuppression/ immunocommitment.	BMT, hematology, oncology, with transplantation, AIDS, neutropenic, primary immune disease (acute rheumatic disease) patients. Check medical records.

Figure 2. Scoring Instructions.

(transplantation of hematopoietic stem cells/hematology), Intensive Care Unit for adults, Neonatal Intensive Care Unit, Pediatric Intensive Care Unit, Pediatric Hospitalization, Pediatric Oncology and Psychiatric Units, the score was applied daily to all patients for three months. In other clinical and surgical units, the patients were randomly sampled and assessed every thirty days for three months, thus reducing seasonal aspects.

On clinical floors and surgical floors, respectively, 50 % and 35 % of the patients were randomly sampled having different beds evaluated every thirty days, according to a selection plan previously elaborated. The process used the sampling percentage based on the relation between the average number of patients in the units, the relative contribution of the units to the total population hospitalized at the HCPA and the length of stay of patients in the units.

With the maps of the units and the percentage of patients to be included in each unit and in each month, the beds were randomly selected for evaluation within the unit, following a proportional selection of beds.

The following sectors were excluded due to their particular characteristics and/or singular logistic aspects: Emergency, Outpatient Clinic, Chemotherapy Sector for Outpatient Clinic, Radiology, Radiotherapy, Surgical Center for Outpatient Clinic, Hemodialysis, Hemodynamic Center, Short Stay Surgical Unit, Surgical Block, Recovery Room and Obstetric Center.

Score as a risk prediction tool; tool development and testing

The candidate elements to be potentially included in the score were revised in the literature. The adverse drug events were selected as the outcome that could define the required pharmaceutical monitoring. Thus, the previously selected elements to be included in the score were individually correlated with the occurrence of adverse events in a univariate analysis and the significant elements in this first analysis

were submitted to a multivariate analysis to assess their correlation with the occurrence of adverse events. Only relevant elements in the second analysis were included in the score.

Validation

Risk factors selected from literature to be included in the score were: number of drugs (polypharmacy, defined as concurrent use more than four drugs), high alert medication; use of total parenteral nutrition or tube; age (children and elderly); comorbidities (renal, liver, heart and lung) and immunocompromised patients. We defined eight indicators with scores ranging from zero to four and the sum was categorized as high risk ≥ 9, moderate 5-8 and low ≤ 4. The interobserver agreement was assessed in a subsample using the Kappa statistical. The agreement with the other items was analyzed through the use of McNemar test.

Statistical Aspects

A database was created in EPI INFO version 3.3.2 to analyze the obtained data. Data evaluation was made in a descriptive manner, the significance level of 0.05 was considered and the chi-square test was employed. Data analysis was made by means of SPSS 16.0.

RESULTS

Table 1 shows the general characteristics of the sample. The score was applied to 1442 patients; 398 (27.6 %) of them presented high risk, 612 (42.4 %) moderate risk and 432 (29.9 %) low risk (Table 2). When analyzing data sorted by age, we found 577 patients at 0 to 14 years of age, 588 at 15 to 65 years of age and 277 patients above 65 years of age. Table 2 shows the score by age group.

In relation to the number of drugs prescribed, 462 patients had the prescription of 0 to 5 drugs: 318 (68.8 %) patients with low score, 139 (30.1 %) with moderate score and 5 (1.1 %) with high score. The use of 11 to 15 drugs was determined in 293 patients: 6 (2.0 %) with low score, 102 (34.8 %) with moderate score and 185 (63.1 %) with high score. The use of more than 16 drugs was observed in 136 (9.4 %) of the patients.

The units identified as high risk were: Pediatric Oncology and Intensive Care Unit for adults and the Pediatric Intensive Care Unit (P< 0.001). Psychiatric Unit and Pediatric Hospitalization presented low risk (P< 0.001), and the units of moderate score were the clinical/surgical units, the protected environment units and the Neonatal Intensive Care Unit (P< 0.001) (Table 3).

Regarding endovenous drugs, the surgical units, the Pediatric Oncology Unit, the Neonatal Intensive Therapy Care Unit, the Intensive Therapy Care Unit for adults and the Pediatric Intensive Care Unit presented the highest number of endovenous drugs prescribed, with 82.7 %, 98.6 %, 87.9 %, 94.9 % and 98.4 %, respectively.

Characteristic		**n**	**%**
Age (years)	0-14	577	40.0
	15-65	588	40.8
	> 60	277	19.2
Drugs prescribed/patient	0-5	462	32.0
	6-10	551	38.2
	11-15	293	20.3
	≥16	136	9.4
Endovenous drugs	None	409	28.4
	1-3	546	37.9
	4 or more	486	33.7
Use of potentially harmful drugs	Did not use any	688	47.7
	1	328	22.7
	2 or more	426	29.5
Nutritional support	Patient uses a tube	320	22.2
	Patient uses Total Parenteral Nutrition (TPN)	60	4.2
Relevant clinical problems	Renal and/or hepatic problems	215	14.9
	Cardiac and/or pulmonary problems	338	23.4
	Immunosuppression and/or immunocommitment	283	19.6

Table 1. Sample characteristics (n = 1442).

N (%)	Age group (years)	Risk (%)		
		Low	Moderate	High
577 (40.0)	0-14	214 (37.1)	244 (42.3)	119 (20.6)
588 (40.8)	15-65	185 (31.5)	229 (38.9)	174 (29.6)
277 (19.2)	> 65	32 (11.5)	139 (50.2)	106 (38.3)

Table 2. Risk classification by age group (n = 1442).

Risk	n (%)	Unit
High	398 (27.6)	Pediatric Oncology Pediatric Intensive Care Unit Intensive Care Unit for adults
Moderate	612 (42.4)	Clinical and surgical units Protected Environment Unit Neonatal Intensive Care Unit
Low	432 (29.9)	Pediatric hospitalization Psychiatric Unit

Table 3. Risk classification according to the unit (n = 1442). Chi-square test, P < 0.001.

Clinical problems	Risk	N (%)
Renal and/or hepatic problems	High	108 (50.2)
	Moderate	82 (38.1)
	Low	25 (11.6)
Cardiac and/or pulmonary problems	High	208 (61.5)
	Moderate	119 (35.2)
	Low	11 (3.3)
Immunosuppression and/or immunocommitment	High	149 (52.6)
	Moderate	119 (42.0)
	Low	15 (5.3)

Table 4. Risk according to clinical problems (n = 1442). Chi-square test, P < 0.001.

In the group of patients with renal and/or hepatic problems, 58.6 % took at least one potentially harmful drug (PHD), while 51 % of non-renal patients did not take any (P = 0.043). In the group of patients with cardiac and/or pulmonary problems, 77.2 % used at least one PHD in relation to 44.6 % of non-pulmonary patients (P< 0.001) and in the group of immunosuppressed and/or immunodeficient patients, 67.5 % used at least one PHD in relation to 48.5 % of the other groups (P< 0.001) (Table 4).

Considering the total of 283 immunosuppressed patients , 15 (5.3 %) presented low score, 119 (42.0 %) moderate score and 149 (52.6 %) low score. Among the 215 patients with renal and/or hepatic problems, 25 (11.6 %) had low score, 82 (38.1 %) moderate score and 108 (50.2 %) high score, and among the 338 patients with cardiac and/or pulmonary problems, 11 (3.3 %) presented low score, 119 (35.2 %) moderate score and 208 (61.5 %) high score (P< 0.001) (Table 4). On the validation, it was administered by two independent observers in 145, within 12 hours. The kappa coefficient was 0.89. The items of disagreement were number of medications (P = 0.04), use of potentially dangerous drug (P = 0.01).

DISCUSSION

Different indicators of PDRM (preventable drug-related morbidity) risk have been studied in Europe, United States and Canada, in community pharmacies [16]. However, in the hospital segment, there is no pharmaceutical instrument to assess hospitalized patients. According to the results obtained in this study, some areas - identified as high risk - should be monitored by a clinical pharmacist. The areas identified as high risk were: Intensive Care Unit for adults, Pediatric Intensive Care Unit and Pediatric Oncology. The moderate risk units were: clinical units, surgical units, protected environment units and Neonatal Intensive Care Unit. The low risk units were: Pediatric Hospitalization and Psychiatric Unit.

Contrary to all expectations for the NICU, the high number of endovenous drugs prescribed was not a decisive factor to classify it as high risk. In the Pediatric Hospitalization Unit, 61.4 % of the patients had more than one endovenous drug prescribed, but the unit was classified as low risk. The same happened in the PEU, as the patients present a peculiarity: they have a longer length of stay and, due to the treatment, the score ranges from moderate to high.

Studies show that the number of drug-related problems per patient increases linearly with the number of drugs used, identifying polypharmacy as a potential risk for the occurrence of these problems [2].

It should be mentioned that, when calculating the number of oral and endovenous items prescribed in the drugs, all "if required" items were considered, except for Dipyrone, Paracetamol and Metoclopramide, because these drugs are present in most prescriptions, which would result in false high scores to patients. Regarding the scores attributed to each age group, the analysis observed that the moderate risk predominated in the age groups. In addition, it was observed that patients with clinical problems (58 % of the sample) used at least one PHD, with all classes classified as high score.

This instrument, randomly applied to patients in the study period, considered the drug therapy related to the number of drugs prescribed, administration method, use of PHD, nutritional support, age and clinical problems relevant to drug metabolism, absorption and excretion. The instrument selects the priority level of monitoring for the patients' drug therapy and frequency of drug interactions, incompatibilities and adverse reactions.

In this study, the patients with high risk factors requiring monitoring priority were defined as *high risk*. Intermediate patients requiring monitoring, but not on emergency basis, were considered as *moderate risk,* and the patients that should be only observed and monitored were classified as *low risk*. The score was applied only once to each patient during the hospitalization period. However, a periodicity should be established in the hospital routine, due to the characteristics of each area.

CONCLUSION

Regarding direct pharmaceutical care requirement, the score may be used to characterize risk groups. The score is expected to help hospital pharmacists direct their pharmaceutical attention more adequately and broadly.

The score is expected to be a tool to reduce occurrences of ADR, with the detection of at-risk population, and establish a more rigorous monitoring of patients at higher risk. Other aspects to improve care quality and functionality, such as optimization of human resources, may also be achieved. The validation in other circumstances may confirm its value in a broader context.

Acknowledgements. To Fundo de Incentivo à Pesquisa (FIPE) of Hospital de Clínicas de Porto Alegre for financial support.

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