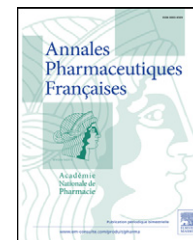




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ORIGINAL ARTICLE

Drug-related problems identified by clinical pharmacist's students and pharmacist's interventions

Les problèmes liés aux médicaments identifiés par des étudiants de pharmacie clinique et les interventions pharmaceutiques

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KEYWORDS

Drug-related problems;
Prospective survey;
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Summary

Background. — Drug-related problems constitute a major public health problem, because of their consequences on morbidity, mortality and cost.

Patients and methods. — A 6-month prospective study was conducted, including hospitalized patients in the internal medicine ward of the University Hospital of Beirut, in order to identify drug-related problems by clinical pharmacist's students participating in routine medical rounds, to assess the characteristics of patients presenting these drug-related problems and to analyze pharmacist's interventions.

Results. — Ninety patients presenting drug-related problems were identified. Thirty-two percent were hydro-electrolytic problems and 24% gastrointestinal. Cardiovascular drugs were the most frequently implicated (44%), followed by anticoagulants (17%) and corticosteroids (14%). The most commonly identified drug-related problems were drug interactions (37%), over-dosage (28%), non-conformity to guidelines or contra-indications (23%), underdosage (10%) and improper administration (2%). The clinical pharmacist's interventions consisted of dose adjustment (38%), addition drugs (31%), changes in drugs (29%) and optimization of administration (2%).

Discussion and conclusion. — To decrease the risk of drug-related problems, drug treatment requires physicians to abide by prescribing recommendations, notably in elderly patients, as well as pharmacists' effective intervention at all levels. Routine participation of clinical pharmacists in clinical medical rounds facilitates the identification of drug-related problems and may prevent their occurrence.

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MOTS CLÉS

Problèmes liés aux médicaments ;
Enquête prospective ;
Étudiants de pharmacie clinique ;
Médecine interne ;
Interventions pharmaceutiques

Résumé

Introduction. — Les problèmes liés aux médicaments constituent un problème majeur de santé publique, tant par ses répercussions en termes de morbi-mortalité, que de coût.

Patients et méthode. — Une étude prospective de six mois a été menée par des étudiants de pharmacie clinique et incluant les patients hospitalisés aux services de médecine interne du CHU de Beyrouth, dans le but d'identifier les problèmes liés aux médicaments, d'évaluer les caractéristiques des patients présentant ces problèmes et d'analyser les interventions pharmaceutiques.

Résultats. — Quatre-vingt-dix patients développant des problèmes liés aux médicaments ont été recensés. Trente-deux pour cent étaient des problèmes hydro-électrolytiques et 24 % gastro-intestinaux. Les médicaments cardiovasculaires étaient les plus fréquemment impliqués (44 %), suivis par les anticoagulants (17 %) et les corticoïdes (14 %). Les problèmes liés aux médicaments les plus fréquemment identifiés étaient : interactions médicamenteuses (37 %), surdosage (28 %), non conformité aux référentiels et contre-indications (23 %), sous-dosage (10 %) et administration inappropriée (2 %). Les interventions pharmaceutiques consistaient en une adaptation posologique (38 %), ajout de médicaments (31 %), changement de médicaments (29 %) et optimisation des modalités d'administration (2 %).

Discussion et conclusion. — Pour diminuer le risque de problèmes liés aux médicaments, le traitement médicamenteux suppose l'adhésion des prescripteurs à des recommandations de prescriptions et de suivi biologique, ainsi que l'intervention efficace de la part des pharmaciens à tous les niveaux. La participation des pharmaciens cliniciens aux tournées médicales facilite l'identification des problèmes liés aux médicaments et peut éviter leur survenue.

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Introduction

Drug-related problems (DRPs) constitute a major public health problem, because of their consequences on morbidity, mortality and cost. According to the literature, they would affect 4 to 22% of hospitalized patients on a given day [1]. Discrepancy within these figures can be explained by specificity of explored hospital structure and ward type. A cohort study, conducted in the USA, shows that the prevalence of DRPs considered clinically important was 79.7% of patients, including therapeutic duplications in 54.6% of patients, dose form optimization in 29.7%, and inappropriate uncoordinated care in 25.3% [2].

According to the French Society of Clinical Pharmacy (SFPC), a DRP is defined as "an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes" [3].

The objective of our study is to identify the DRPs in patients hospitalized into internal medicine ward, by clinical pharmacist's students participating in routine medical rounds, to assess the characteristics of patients presenting these DRPs and to analyze pharmacist's interventions.

Patients and methods

We conducted a prospective study over a period of 6 months (November 1st 2009 to April 30th 2010), including hospitalized patients in the internal medicine ward of the University Hospital of Beirut and presenting DRPs whatever is their chief complaint. We chose the internal medicine ward because of diversity of cases and of drugs that could be

used. We excluded patients hospitalized in other services, those admitted for voluntary drug intoxication, those who refused to participate to the study, and those who could not be interviewed for medical reasons.

DRPs were identified by clinical pharmacist's students during their participation to the morning round performed by physicians on the internal medicine ward patients. Identification of DRPs was realized by reviewing and analyzing all medication orders, administration sheets, laboratory and diagnostic test results, and pathophysiological status. Clinical pharmacist's students (Pharm D Clinical Pharmacist's students) were specially trained for this task before they started their rotation. DRPs were reviewed and approved by two clinical pharmacists (Pharm D, PhD Clinical Pharmacy) using a structured order review (SFPC instrument) [4,5]. The file number of patient was registered in order to review the computerized file, interview the patient and retrieve the necessary information for the study. The computerized patient files were used by clinical pharmacist's students to validate drug prescriptions and administrations. Validation is characterized by the formulation of pharmaceutical interventions defined as: any proposal to modify drug therapy initiated by the pharmacist [6]. It includes the identification, prevention and resolution of problems related to drug therapy.

The research support was a directive questionnaire, constituted of five parts:

- patient's characteristics, including age, sex and medical history;
- drug treatment, describing the drugs that were administered to the patient during hospitalization period: drug name, indication, dose, schedule, duration, biological monitoring and associated drugs;

Table 1 Characteristics of patients with drug-related problems (DRPs).*Caractéristiques des patients présentant des problèmes liés aux médicaments.*

Variables	n (%)
Age (≥ 65 years)	55 (61)
Sex (male)	49 (54)
History of cardiac pathology (myocardial infarction, hypertension, heart failure, atrial fibrillation, valvulopathy, valve replacement, arrhythmia)	62 (69)
History of diabetes (insulin-dependent, non-insulin dependent)	34 (38)
History of cerebral pathology (ischemic stroke, hemorrhagic stroke)	23 (26)
History of gastrointestinal pathology (gastroduodenal ulcer, gastro-esophageal reflux)	16 (18)
History of renal insufficiency (creatinine clearance < 30 ml/min)	5 (6)

- the DRPs part described the type of DRP, its localization, clinical manifestations, as well as involved drugs;
- DRPs were reviewed by using a structured order review (SFPC instrument) [4,5]. This form includes the identification of the DRPs (10 items) [7] and the pharmacist's interventions (seven items) [8]. The retained criteria were the following:
 - non-conformity to guidelines or contra-indications: presence of a pathophysiological status that counter-indicates the use of one or more drugs. Contra-indications evaluation was carried out according to an international reference [9],
 - drug interactions: presence of drug interactions where a precaution is recommended but was not taken into account, that discourage or contra-indicate the use of one or more drugs. Drug interactions were evaluated according to the "Drug Interaction Facts" and "Thésaurus des interactions médicamenteuses" [10,11],
 - overdosage or underdosage: prescription of a dose that is superior or inferior to the mean daily recommended dose for an adult [9]. It includes the overdosage when the dose is not adjusted according to the creatinine clearance,
 - improper administration: schedule of drug intake was not optimal or not respected;
- pharmacist's interventions: pharmacist's interventions were formulated by clinical pharmacist's students, reviewed and approved by two clinical pharmacists

(Pharm D, PhD Clinical Pharmacy) according to the structured order review (SFPC instrument) [5,8].

Statistical analysis

A descriptive analysis was carried out on variables involved in DRPs, using the SPSS software, version 14.0.

Results

Five hundred seventy-two patients were hospitalized during the 6-month study period in the internal medicine ward. Of these, 90 patients developing DRPs (41 women and 49 men) were identified, representing 15.7% of hospitalized patients. Sixty-one percent of these patients were aged 65 or more. In Table 1, we present the characteristics of patients who developed DRPs. Among medical history characteristics, we found cardiovascular pathologies (69%) and diabetes (38%).

Twenty-nine cases of DRPs (32%) presented as hydro-electrolytic problems: 13 cases of hypokalemia and 10 cases of hyperkalemia; 24% were gastrointestinal problems, including 19 cases of digestive hemorrhage. Cardiac problems were found in 11 cases (12%), including five hypertension, five hypotension and one case of bradycardia. Renal damage was also found (9%): five cases of hematuria and three cases of kidney failure. In the five cases (6%) of confusion and general fatigue, a cerebral hemorrhage was diagnosed. One lung manifestation was also found:

Table 2 Classification of drug-related problems (DRPs) and clinical manifestations.*Classification des problèmes liés aux médicaments en fonction des manifestations cliniques.*

Clinical manifestations	Frequency	Percentage
Hydro-electrolytic manifestations	29	32
Gastrointestinal manifestations	22	24
Cardiologic manifestations	11	12
Metabolic and endocrine manifestations	9	10
Renal manifestations	8	9
General fatigue and confusion	5	6
Hematologic manifestations and hemostasis disturbances	3	3
Dermatologic manifestations	1	1
Neurologic manifestations	1	1
Pneumological manifestations	1	1
Total	90	100

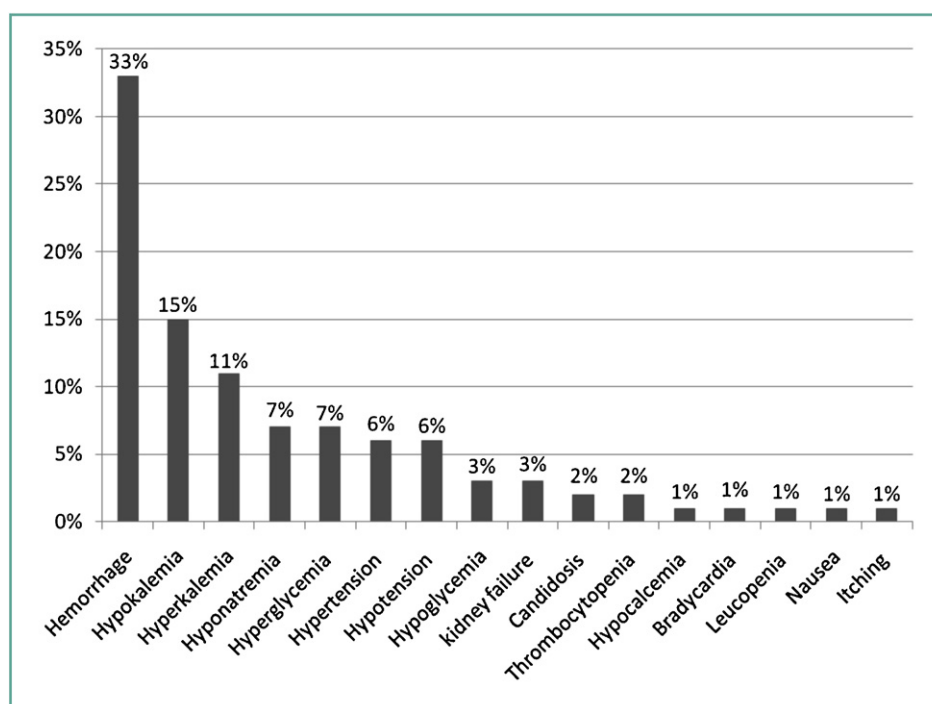


Figure 1. Classification of drug-related problems (DRPs) and clinical signs.
Classification des problèmes liés aux médicaments en fonction des signes cliniques.

alveolar hemoptysis. We present the clinical manifestations in Table 2, while the Fig. 1 shows the distribution of DRPs according to clinical signs.

Cardiovascular drugs were the most involved in occurrence of DRPs, with a percentage of 44%, followed by anticoagulants (17%), and corticosteroids (14%). Table 3 presents DRPs by drug class.

The most commonly identified DRPs were drug interactions (37%), overdosage (28%), non-conformity to guidelines or contra-indications (23%), underdosage (10%) and improper administration (2%) (Fig. 2).

The pharmacist's interventions consisted of dose adjustment (38%), addition drugs (31%), changes in drugs (29%) and

optimization of administration (2%) (Table 4). The acceptance rate of pharmacist's intervention was 96%.

Discussion

Patients aged 65 years and more seem more exposed to DRPs (61% versus 39% of patients aged less than 65 years); this confirms that DRPs likelihood increases with age [12]. In fact, the role of age in DRPs occurrence is more and more established. This is probably not due to age itself but to frequent comorbidity of aged patients. A male predominance in patients with DRPs was found in our study sample. Available results in the literature regarding the role of sex are discordant; the increase in frequency of DRPs in men [13,14] is not found by all researchers [15–17].

Among medical history examined in the study, we found that the risk of DRPs exists mainly in patients with cardiovascular disease. The presence of several diseases such as myocardial infarction, atrial fibrillation, heart failure, ischemic stroke and others, requiring polymedication and the modification of pharmacokinetic parameters (particularly in aged patients), implies a population with multiple exposure to iatrogenicity, which can be a consequence of pharmacokinetic or pharmacodynamic drug interactions. In the latter case, there are precautions to take for certain drugs and dose adjustment to make, in order to decrease the iatrogenic risk.

Thirty-two percent of DRPs were hydro-electrolytic problems, 24% gastrointestinal, 12% cardiac, and 9% renal. These results resemble those found by other researchers, showing a predominance of hydro-electrolytic problems

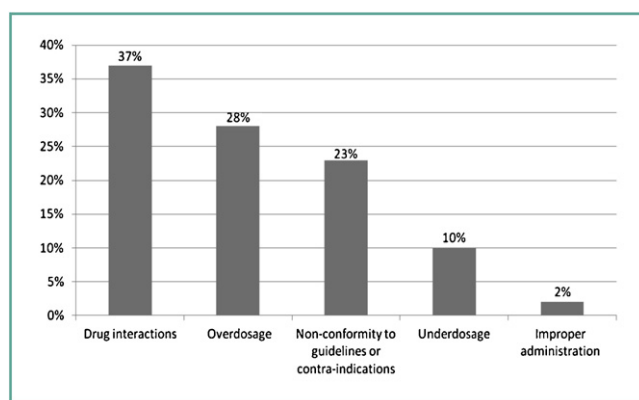


Figure 2. Identified drug-related problems (DRPs).
Les problèmes liés aux médicaments identifiés.

Table 3 Drug-related problems (DRPs) per drug class.
Les problèmes liés aux médicaments par classes médicamenteuses.

Drug class and most common used drugs involved	Frequency	Percentage
Cardiovascular drugs: furosemide (<i>n</i> = 21), candesartan (<i>n</i> = 2), valsartan (<i>n</i> = 2), amiodarone (<i>n</i> = 2), spironolactone (<i>n</i> = 1), telmisartan (<i>n</i> = 1), ramipril (<i>n</i> = 1), irbesartan (<i>n</i> = 1), perindopril (<i>n</i> = 1), lisinopril (<i>n</i> = 1)...	40	44
Anticoagulants: acenocoumarol (<i>n</i> = 13), heparin (<i>n</i> = 2)	15	17
Corticosteroids: methylprednisolone (<i>n</i> = 7), dexamethasone (<i>n</i> = 4), prednisone (<i>n</i> = 2)	13	14
Non steroidal anti-inflammatory drugs: naproxen (<i>n</i> = 3), ketoprofen (<i>n</i> = 2), diclofenac (<i>n</i> = 1), meloxicam (<i>n</i> = 1)	7	8
Antiplatelet drugs: aspirin (<i>n</i> = 4), tirofiban (<i>n</i> = 1)	5	6
Anti-infectious drugs: ampicillin (<i>n</i> = 1), cefazolin (<i>n</i> = 1), ofloxacin (<i>n</i> = 1), acyclovir (<i>n</i> = 1), valacyclovir (<i>n</i> = 1)	5	6
Antidiabetic drugs: insulin (<i>n</i> = 3), glimepiride (<i>n</i> = 1)	4	4
Other	5	4

among iatrogenic events collected prospectively in internal medicine and infectious diseases ward [18], while cardiac problems come second and digestive problems only represent 2% of the DRPs [18]. The high frequency of digestive problems in our study is mainly due to the high number of digestive hemorrhage. This frequency may be related to the underlying high rate of use of non-steroidal anti-inflammatory drugs, antivitamin K, antiplatelets in the internal medicine wards.

Neurological manifestations constitute an important part of DRPs in several studies [18–20], while they only constituted 6% of DRPs in our study. This can be due to the low prescription of neuropsychiatric drugs (anticonvulsants, antidepressive agents...) in internal medicine wards of the University Hospital of Beirut.

Cardiovascular drugs were the most frequently implicated in DRPs occurrence (44%). This percentage is similar to the one obtained by Bruneau and collaborators on older individuals [19]. Other studies [18,20,21] found similar percentages. A French study also reported that cardiovascular drugs were the most frequently implicated in DRPs (22,2%) [22]. DRPs due to cardiovascular drugs are mainly localized at the plasma level (hyponatremia, hypokalemia...) and the cardiac level (hypotension, hypertension...). The second involved drug group was anticoagulants (17%), similar to the results of Gurwitz [23]. Antivitamin K comes first with 13 cases (14% of DRPs), followed by heparins (3%). Another study carried out 12 years ago at the American University Hospital of Beirut showed that anticoagulants were

responsible of 7.4% of DRPs [24]. In our study, the clinical manifestation induced by anticoagulants is digestive, renal and cerebral hemorrhage. Adhesion of prescribers with recommendations of adaptation to older subjects limits the incidence of overdosing and its complications [25].

Antiinfectious drugs were responsible of 6% of DRPs. This figure is lower than the one found by other studies [1,13,26]. This may be explained by a better application of guidelines in case of antiinfectious use in the University Hospital of Beirut.

In our study, we found that drug interactions were involved in 37% of DRPs cases, overdosage in 28%, non-conformity to guidelines or contra-indications in 23%, underdosage in 10%, and improper administration in 2% of cases. Our results can be compared with those reported in a French study, where non-conformity to guidelines or contra-indications were in 29.5% of cases, improper administration in 19.6%, drug interactions in 16.7% and overdosage in 12.8% [22].

We used the instrument of identification and analysis of pharmacist's interventions developed by the SFPC as it is faster than that of Pharmaceutical Care Network Europe (PCNE) that requires more information [27]. The SFPC instrument is best regarding our study because among DRPs some problems cannot be classified with PCNE while all can be classified with SFPC. These problems concern those related to improper administration. Moreover some researchers have compared both methods and found that the coding of pharmacist's interventions during medical visits can be performed simply and nearly complete with the SFPC instrument but not with PCNE instrument [28].

The main interactions we found in our study involved drugs that should not be co-prescribed, such as: acenocoumarol and non-steroidal anti-inflammatory drugs (causing hematuria), acenocoumarol and other potentializing drugs such as amiodarone (enzymatic inhibitor that caused a cerebral hemorrhage and patient's death), acenocoumarol and antibiotics (causing alveolar hemoptysis). Gurwitz and collaborators showed a similar importance of

Table 4 Clinical pharmacist's interventions.
Les interventions pharmaceutiques.

Patient care	Frequency	Percentage
Dose adjustment	34	38
Addition drugs	28	31
Changes in drugs	26	29
Optimization of administration	2	2

acenocoumarol in DRPs incidence, while heparin is only involved in 1% of cases [23]. Antibiotics are commonly used in elderly patients and classically identified as antivitamin K potentiating drugs [29]; the occurrence of hemorrhage when antivitamin K was associated with antibiotics can be explained by destruction of the intestinal flora and decrease in the synthesis of vitamin K, decrease the metabolism of antivitamin K by enzymatic inhibition (fluconazole, itraconazole and erythromycin) or decrease the protein-binding (fluoroquinolones) [30]. Siguret and collaborators showed that 69% of overdosing cases are associated with antivitamin K potentiating drugs [31], particularly anti-infectious drugs and amiodarone [31]. Monitoring INR should be increased in these high risk situations.

Pharmacist's interventions included dose adjustment (38%), addition drugs (31%), changes in drugs (29%) and optimization of administration (2%).

The correction of 30 cases of hemorrhage necessitated vitamin K administration in eight cases, red blood cells transfusion in six cases, and fresh frozen plasma transfusion in six cases. In our study, the treatment of hemorrhagic DRPs is concordant with the Afssaps recommendations [32].

In our study, the pharmacist's interventions were formulated by clinical pharmacists directly to physicians during their participating in medical rounds. The acceptance rate of pharmacist's interventions was 96%. Our study is comparable to a study conducted in England and showed an acceptance rate of pharmacist's interventions of 96% [33]. Another study showed that the acceptance of pharmacist's intervention by physicians was 98% [34]. This high acceptance showed the clinical relevance of pharmacist's interventions during the medical visits and the evolution of physician-pharmacist relationship.

Suboptimal professional practice found in this study that led to DRPs can be reduced by physicians, pharmacists and nurses' involvement. For physicians, adherence to prescription guidelines may reduce DRPs incidence, particularly when adapted to aged patients. Recognition by prescribers of aging effect on drugs kinetics is of particular interest to reduce DRPs. Moreover, besides adequate dosing, respecting the right intake schedule by the nurse can prevent underdosing or overdosing. Thus, iatrogenic risk should be continuously evaluated in this vulnerable population, particularly in case of drug interactions. Other preventive measures that could be suggested by our study include the precise evaluation of pathologic status and therapeutic priority establishment, dosing adaptation according to renal, hepatic and cardiac function, and taking into consideration drug interactions. Continuous education of medical, nursing and pharmaceutical professionals and therapeutic evaluation of professional practices can also contribute to the quality and security of care, in reference with validated good practice measures [35].

The presence of a clinical pharmacist on wards could be advantageous in these situations: He could serve as a counselor to the physician [36], and for prescription validation and DRPs prevention [37,38]. Participation of a clinical pharmacist to the round could prevent more than 60% of DRPs [37]. His counseling for physicians and nurses improves the clinical evolution of the hospitalized patient [39] and eventually

decreases cost, duration of hospitalization and mortality [40–42]. The concept of clinical pharmacy is applicable in Lebanon for several reasons: the incidence of DRPs is not different from that in Western nations [24], 40% of drug orders were shown to comprise at least one medication prescribing error [43], physicians and nurses are aware of the importance of clinical pharmacy [44], pharmacists have enough education and are willing to work as clinical pharmacists [45] and hospital official accreditation by the Lebanese Ministry of Health requires the presence of clinical pharmacists [46].

Conclusion

Our study shows that many factors are associated with DRPs occurrence in hospitalized patients, including inappropriate adaptation of security rules during prescription, dispensing and drug administration. Drug treatment benefit supposes adherence to prescription, administration and monitoring guidelines, particularly in elderly patients; the efficient intervention of pharmacist at all levels is suggested. The importance of clinical pharmacy activities can be demonstrated by the high acceptance rate of pharmacist's interventions, which may be related to the formulation of these interventions by clinical pharmacists directly to physicians during their participating in medical rounds. In this context, routine participation of clinical pharmacists in clinical medical rounds facilitates the identification of DRPs and may prevent their occurrence.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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