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DETECTION AND ANALYSIS OF POSSIBLE INTERACTIONS BETWEEN DRUGS PRESCRIBED AT HOSPITAL DISCHARGE

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ABSTRACT

Interaction between drugs constitutes a frequent cause of adverse drug reaction. The aim of this study, was to provide an analysis of potential drug interactions. The study groups were 225 patients from the dialysis unit and 519 patients from the heart failure centre. Discharge prescriptions from the two units were collected for six months during 2011. In the heart failure centre, 74% of patients received prescriptions for drug combinations that may have adverse interactions. The most frequent and important potential interactions concerned furosemide with enalapril,17%, and acetylsalicylic acid with metoprolol, 15%. In the dialysis unit, 19% of patients received prescriptions that may have adverse interactions. Two examples were algeldrate with amlodipine, 6%, In 1.3% of patients increase in INR occurred owing to interactions. The results have revealed particularly high risk for potential interactions in heart failure centre patients because of the prescription of many drugs and because of the types of these drugs.

Keywords:- Interaction between drugs; adverse drug reaction; prescribed therapy.

INTRODUCTION

Drug–drug interactions (DDIs) are of clinical importance since they constitute a frequent cause of adverse drug reactions (ADRs) during therapy and may result in the patient's stay in hospital being prolonged or readmission being required. It has been estimated that 6–30% of all ADRs are due to DDIs. From a review of nine studies the incidence of readmission caused by DDIs was 2.8%. This adds up to 245,280 admissions per year in a nation the size of the United States of America at a yearly cost of 1.3 billion dollars [1].

Identification of potential DDIs is not easy given the complexity of the matter, and even the most experienced of clinicians may have difficulty in remembering all the possible interactions [2]. Potential interactions are frequently identified through screening linked to the dispensing of drugs. However, the usefulness of screening for DDIs in normal clinical practice in the reduction of morbidity and mortality has not been adequately evaluated [3]. The literature confirms that there is an increased risk of developing ADRs as the number of drugs used and the patient's age increase [4-5].

This study comprised a qualitative–quantitative analysis of potential DDIs present in prescribed therapy at hospital discharge. The aim was to provide an analysis of the problem of potential DDIs, the identification of which was one of the monitoring tasks carried out by the hospital pharmacy.

Many service units of the hospital order discharge medications directly from the hospital pharmacy. Discharge prescriptions from the dialysis unit and from the heart failure centre were chosen for the study. Compared with other services, these two have a high risk of possible DDIs, given the types of drugs involved, the age group of the patients and the complexity of the pathologies treated.

MATERIALS AND METHODS

Patients and data collection

Data related to the discharge prescriptions for 519 patients from the heart failure centre and for 225 patients from the dialysis unit were collected for six months from January through June, 2011. Most of the patients lived in the Province of Ferrara (about 358,000 residents).

Personal data of the patient, information on the qualitative-quantitative description of the drugs delivered and their potential DDIs, anatomical therapeutic chemical (ATC) classification of the drugs and the amount of medicine dispensed were gathered from the pharmacy records of the University Hospital of Ferrara.

Data analysis used the following parameters: Patient gender; patient age group; clinically important potential DDIs of the most frequently prescribed drug combinations; and percentage of single categories of drugs according to ATC.

Analysis of potential DDIs

Potential DDIs were evaluated with Drug-Reax, a computerised drug interaction system (Micromedex ®). This program provides information on the potential clinical consequence or ADR resulting from a DDI and classifies severity into three categories: major, the interaction can be life-threatening and require medical intervention to minimize or prevent serious adverse effects; moderate, the interaction may cause a worsening the patient's condition and require a change in therapy; minor, the interaction would have limited clinical effect.

Data analysis

Results are expressed as proportions or as means (± SD). Chi-square statistics were used for categorical comparisons. A two-sided *P* value less than 0.05 was considered statistically significant. Data were analysed with SPSS for Windows version 10.

RESULTS AND DISCUSSION

Heart Failure Centre

In this unit 386 patients (74%) out of a total of 519 received prescriptions for drugs that may cause clinically important DDIs (Table 1).

Among the patients, there was a preponderance of male subjects, 72%, compared with 28% females. The number of drugs prescribed for each patient varied from a minimum of one to a maximum of fourteen (mean = seven). The drugs were classified in accordance with ATC. The most frequent was Group C (cardiovascular system), 71.09% of all prescriptions, followed by Group B (blood and blood forming organs), 16.38%, Group A (alimentary tract and metabolism), 4.15%, Group M (musculoskeletal system), 3.11%, Group R (respiratory system), 1.86%, Group H (systemic hormonal preparations, excluding sex hormones and insulins), 1.31%, and

Group S (sensory organs), 1.31%:

Patients aged 70–80 years represented the most frequent group for potential DDIs. Out of 386 patients, 155 were in this age group. The mean age was 71 years. The most frequently found potential major interactions concerned nine drugs (Table 2).

In 88 patients a potential interaction for furosemide with enalapril was found in 68 males compared with 20 females. A potential interaction for warfarin with simvastatin was found in 40 patients, 4 were female and 36 were male. Potential interaction for amiodarone with warfarin involved 42 male patients and 11 female patients . [6-11].

Clinically important drug interactions

It is interesting to note that when these clinically important potential DDIs were considered, the percentage of patients involved decreased from 74.4% to 66.3%. Among the nine most frequently found major potential DDIs, six corresponded to the potential DDIs that most frequently appeared in the sample population.

Clinical relevance of some important drug interactions

We evaluated for major drug interactions in treatment at the heart failure centre. Nineteen (3.7%) patients treated with warfarin prescribed concomitantly with allopurinol or with amiodarone needed change of the dosage of anticoagulant due to the DDI that can cause increased bleeding time. One (0.2%) patient on warfarin prescribed in combination with amiodarone or with allopurinol presented with bleeding caused by the interaction. Thirteen (2.5%) patients showed severe hyperkalaemia due to the interaction between potassium and ramipril. Five (1.0%) patients experienced toxic effects of digoxin, such as nausea, vomiting, and cardiac arrhythmias due to digoxin interaction with furosemide. In practice, there have been relevant clinical events due to DDIs in 38 (7%) patients followed at the heart failure centre.

Dialysis Unit
In this unit, 43 patients out of a total of 225 (19%) received prescriptions that may cause clinically important DDIs (Table 3).

Most of the patients were male, 70%, and 30% were female. The age group most at risk for potential DDIs was the 50–60 year group, followed closely by the 60–70 year group. Mean age was 62 years. The ATC classifications show that the most frequently prescribed drugs belongs to Group L (antineoplastic and immunomodulating agents), 23.05% of all prescriptions, followed by Group B (blood and blood forming organs), 22.81%, Group A (alimentary tract and metabolism), 19.32%, Group C (cardiovascular system), 18.02%, Group H (systemic hormonal preparations, excluding sex hormones and insulins), 6.86%, Group S (sensory organs), 6.39%, and Group J (anti-infectives for systemic use), 1.43%.

Clinically important drug interactions
When the potential major interactions are taken into consideration, the percentage of patients involved decreases from 19% to 9.3%. Table 4 illustrates the most frequently found potential DDIs. The potential interaction for algeldrate with amlodipine was the most frequent.

Most of the potential DDIs involved a small number of subjects. The observations regarding patient gender and potential DDIs in the heart failure centre patients were also noted for the dialysis unit patients, although the potential DDIs for calcium carbonate with nifedipine and for calcium carbonate with ferrous sulfate showed no difference in the male-female risks. There were relevant clinical events due to DDIs with an increase in International Normalized Ratio (INR) for three patients. The interactions involved were warfarin with simvastatin in two patients and magnesium hydroxide with polystyrene sodium sulfate in one patient.

CONCLUSIONS

The data obtained from this study reveal that the number of patients involved in the problem of potential DDIs is significant. [11] Within the sample population, the frequency of the potential DDIs in relation to the number of patients was 19% (43/225) in the dialysis unit and 74.4% (386/519) in the heart failure centre. The results have revealed that the potential DDIs are a greater problem for the cardiac failure centre patients. The high number and types of drugs that individual patients were prescribed may account for this.

In this study, we detected relevant clinical events due to interactions, with rates of 7.0% (3.43 patients with interactions) in the dialysis unit and 10.0% in the heart failure centre (38/386). From these data, it is clear that the clinical relevance of DDIs is higher for the heart failure centre.

We conclude that the hospital pharmacist has a fundamental role in the identification, analysis or interpretation of DDIs. The pharmacy of the University Hospital of Ferrara intends to promote a project which will provide the hospital pharmacist with a new task. This will involve contacting the doctor who prescribes drug combinations that may have potentially adverse interactions. Although this task has already been introduced, it is still not being systematically carried out. The aim is to make it customary in future. This means that the hospital pharmacist will be expected to report potential adverse interactions and propose possible corrections and/or changes to drug prescriptions in the hope of eliminating, substituting or changing the dosage or mode of administration of drugs that may interact negatively with other prescribed drugs.

COMPETING INTERESTS
The authors declare that they have no competing interests

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Table 1: Characteristics of patients from the heart failure centre.

	Number	%	*P* value
Patients	519	100%	
Males	376	72.5%	
Females	143	27.5%	
Number of the patients per age group (%)			
90–100 years	3	0.6%	
80–90 years	92	17.7%	
70–80 years	208	40.1%	
60–70 years	132	25.4%	
50–60 years	60	11.6%	
40–50 years	13	2.5%	
30–40 years	11	2.1%	
Number of drugs prescribed in a single prescription			
Maximum	14		
Minimum	1		
Mean (SD)	7 (± 3)		
Number of patients with potential DDIs	386	74.4%	<0.01
Number of patients with clinically important potential DDIs	344	66.3%	<0.01
Total number of prescriptions	1096		

Table 2: Potential drug-drug interactions (DDIs) among the most frequent and clinically important drug combinations from the heart failure centre.

Names of drugs often-prescribed in combination	Number of patients with a prescription for both drugs (%)	Severity of DDI risk
furosemide–enalapril	88 (17.0%)	major
acetylsalicylic acid–metoprolol	78 (15.0%)	major
digoxin–furosemide	60 (11.6%)	major
amiodarone–warfarin	53 (10.2%)	major
acetylsalicylic acid–nitroglycerine	53 (10.2%)	moderate
warfarin–simvastatin	40 (7.3%)	moderate
acetylsalicylic acid–amlodipine	38 (7.3%)	moderate
amiodarone–carvedilol	30 (5.8%)	major
potassium–ramipril	28 (5.4%)	major
allopurinol–warfarin	27 (5.2%)	major
spironolatone–ramipril	26 (5.0%)	major
amiodarone–bisoprolol	19 (3.7%)	major

Table 3: Characteristics of patients from the dialysis unit

	Number	%	*P* value
Patients	225	100%	
Males	157	69.8%	
Females	68	30.2%	
Number of the patients per age group (%)			
80–90 years	16	7.1%	
70–80 years	42	18.7%	
60–70 years	63	28.0%	
50–60 years	73	32.4%	
40–50 years	26	11.6%	
30–40 years	5	2.2%	
Number of drugs prescribed in a single prescription			
Maximum	11		
Minimum	1		
Mean (SD)	3 (± 2)		
Number of patients with potential DDIs	43	19.1%	<0.001
Number of patients with clinically important potential DDIs	21	9.3%	<0.001
Total number of prescriptions	663		

Table 4: Potential drug-drug interactions (DDIs) among the most frequent and clinically important drug combinations from the dialysis unit

Names of drugs often prescribed in combination	Number of patients with a prescription for both drugs (%)		Severity of DDI risk
algedrate–amlodipine	13	(5.8%)	major
acetylsalicylic acid–magnesium	9	(4.0%)	moderate
warfarin–simvastatin	9	(4.0%)	moderate
magnesium hydroxide–sodium polystyrene sulfate	6	(2.7%)	major
enoxaparin–nitroglycerine	5	(2.2%)	major
doxazosin–carvedilol	5	(2.2%)	moderate
acetylsalicylic acid–metoprolol	3	(1.3%)	major
nifedipine–carvedilol	2	(0.9%)	major
calcium carbonate–ferrous sulphate	2	(0.9%)	major
calcium carbonate–nifedipine	2	(0.9%)	major

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