Acta Pharm. 55 (2005) 157–167 Original research paper

Prescribing medication errors in hospitalised patients: A prospective study

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The aims of this prospective study were to determine the incidence and types of prescribing medication errors and ways to prevent them from reaching patients. Data were collected from 4951 prescriptions over a 25 week period in 2002. Medication errors were classified as: incorrect dose, incorrect dose interval, duplication of therapy and drug interactions. The medical record analysis was used to compare prescribing with Croatian literature drug data and AHFS first Web version 2 (American Society of Health System Pharmacists). The incidence of medication errors in the entire sample, including all potential drug interactions, was 14.7%. However, as only 8 interactions (out of 356 potentially possible interactions) were assessed as clinically significant, then the total number of all types of medication errors was 379. This resulted in an incidence of 7.7%. Dosage errors were the most frequent errors, followed by incorrect interval, drug duplication and drug interaction. The difference between the incidence of potentially possible and clinically significant drug interactions was quite large (7.2 *vs*. 0.2%). Thus, a critical attitude is necessary when evaluating available data on drug interactions. Our findings point to the need of systematic control of prescribed therapies, which could be ensured by the application of the Unit Dose Drug Distribution System. A medication errors reporting program should be established both at the hospital and at national levels in Croatia.

Received November 29, 2004
Accepted May 23, 2005

Keywords: drug interactions, hospitalised patients, medication errors, prescribing, prospective study

A medication error is defined as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient and consumer (1).

Such events may be related to the professional practice, health care products, procedures, and systems, including prescribing, order communication, product labeling, pa-

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ckaging, and nomenclature compounding, dispensing distribution, administration, education, monitoring and use (2–6).

We distinguish between errors in the planning (»mistakes«) and errors in the execution of the act (»slips«). Slips result from distractions or failure to pay attention at critical moments. Mistakes are more complex and include the rules based on mistakes and knowledge. They arise because of lack of knowledge or because of misinterpretation of the problem.

The Institute for Safe Medication Practices (ISMP) was established in 1994 in the USA as a non-profit organization that works closely with practitioners, regulatory agencies, health care institutions, professional organizations and the pharmaceutical industry to provide education about adverse drug events. In 1995, the USP spearheaded the formation of the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP). Leading national health care organizations are for the first time, meeting, collaborating and cooperating to address the interdisciplinary causes of errors and to promote the safe use of medications.

NCCMERP has reviewed thousands of reports of medication errors. In all cases, the causes are multifactorial, cutting across many lines of responsibility.

Leape and co-workers (7) define broad categories or domains, describing the underlying problems that result in medication errors. They found that 56% of the cases they detected were due to prescription errors and 44% involved delivery and administration.

A comprehensive examination of adverse drug events in two large academic long-term care facilities (8) reports their incidence of 9.8%. Nearly 42% of the observed cases were assessed as preventable. Study findings reinforce the need for a special focus on the ordering and monitoring stages of pharmaceutical care for preventing medication errors.

Medication error can be recognized and used to help prevent future errors. Methods of medication error analysis provide models for the detection and reduction of accidents. Investigations of medication errors have contributed to reducing the rate of their incidence.

The objective of this study was to determine the incidence of medication errors, to identify the types of prescribing medication errors in order to improve the present system of drug distribution in the hospital (floor stock system) by changing to the Unit Dose Drug Distribution System (UDDDS). Thus, clinical pharmacists will be directly involved in the control of prescribed therapy and able to promptly perceive a prescribing error, eliminate it and prevent it from reaching and possibly damaging the health of the patient.

EXPERIMENTAL

Data collection

The occurrence of medication errors was analyzed in a prospective study of prescriptions during a period of 25 weeks in 2002 in different wards of the Clinic of Internal Medicine (Dubrava University Hospital, Zagreb). Patient records were randomly selected and evaluated by a blind process involving a pharmacist and a physician. The pre-

scribed therapy was controlled with regard to drug dose and dosing interval, according to official drug data, duplication of drugs based on their association with the therapeutic drug class, interactions and, separately, clinically significant interactions classified according to AHFS first Web version 2 (9). A total of 4951 randomly chosen medical records for 1303 patients, aged from 20 to 78 years, were examined. Of the total number, 33% of the patients were female and 67% male. The patients were hospitalized for 10.4 days on average. The average number of prescribed drugs per patient amounted to 3.8.

Database for monitoring medication errors

Data for monitoring medication errors were taken from the database of drugs AHFS first Web version 2 (9), Pharmacotherapy manual 3 (10) and Register of Drugs in Croatia (11). The prescribed therapy is listed according to generic names of drugs in the »drug profile« – AHFS first (9), which enables rapid screening of possible significant interactions, classified in three categories according to the severity level: 1 – contraindicated, meaning that the particular drug combination is clearly contraindicated in all cases and should not be dispensed or administered to the same patient, 2 – severe interaction, meaning that action is required to reduce the risk of a severe adverse reaction, and 3 – moderate interaction, meaning to assess the risk to the patient and take action as needed.

Results are expressed as percentage of the confirmed medication errors in relation to the total number of prescribed drugs (prescriptions).

RESULTS AND DISCUSSION

Prescribed therapy was investigated in a prospective study with regard to drug dosage, dosing interval, therapy duplication and possible interactions of the prescribed drugs due to simultaneous application of another drug. Table I shows the medication errors determined, expressed as the number of occurrences and the percentage in relation to the total number of prescriptions. Fig. 1. shows the share of specific medication errors in relation to the total number of medication errors. The share of medication errors according to pharmacotherapeutic groups is presented in Fig. 2. The largest share of medication errors was involved drugs in group C, acting on the cardiovascular system, and

Table I. Types and incidence of observed medication errors in the total number of 4951 prescriptions

	Incorrect drug dose	Incorrect dosing interval	Therapy duplication	All potential drug interactions/Only clinically significant drug interactions	All medication errors/Medication errors including only clinically significant drug interactions
Number of occurrences	168	134	69	356/8	727/379
Incidence (%)	3.4	2.7	1.4	7.2/0.2	14.7/7.7

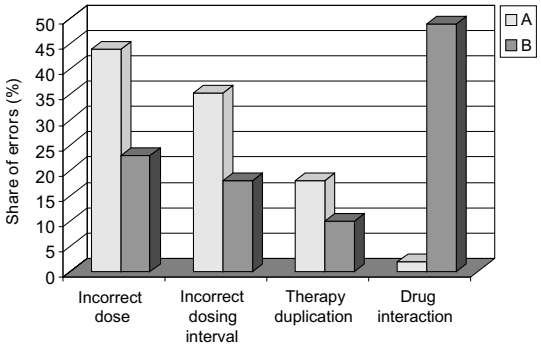

Fig. 1. Share of certain types of prescribing medication errors, including clinically significant drug interactions only (A) and all potential drug interactions (B).

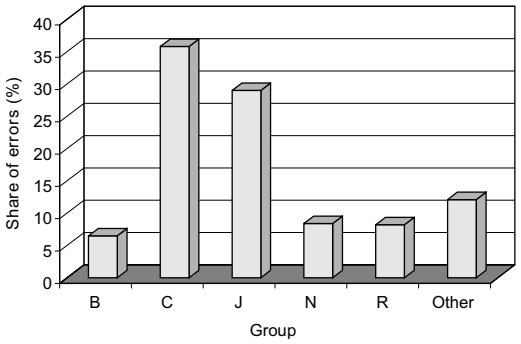

Fig. 2. Share of observed medication errors in relation to the groups of ATC-classification of drugs: B – blood and blood forming organs, C – cardiovascular system, J – anti-infectives for systemic use, N – nervous system, R – respiratory system, other – other groups.

in group J, anti-infective drugs [according to the Anatomical Therapeutic Chemical (ATC) classification of drugs], which is partly proportional to the participation of individual groups of drugs in the total drug consumption expressed in defined daily doses (DDD) per 100 hospital days (Fig. 3).

Table II shows the relation between age of hospitalized patients, share of prescriptions and share of medication errors. Data in Table II show a larger share of older patients in the number of prescriptions, and consequently a higher incidence of medication errors.

The incidence of incorrect drug doses was 3.4% (or 168 cases) of the total number of prescriptions (4951). 29% of the incorrectly prescribed drug doses were overdosed, while 71% were underdosed. About 50% of the errors connected with drug dosing referred to antibiotics, most frequently underdosed.

The incidence of incorrect dosing intervals was 2.7% (134 cases) of the total number of prescriptions. In more than 14% of those cases the dosing interval was not recorded at all!

During the study, prescribing of drugs from the same pharmacotherapeutic groups (duplication of therapy) was observed in 69 cases, or 1.4% of the total number of prescriptions. The most frequent simultaneously prescribed drugs were calcium channel blockers, *e.g.* nifedipine and verapamil. Frequent duplication of therapy with non-ste-

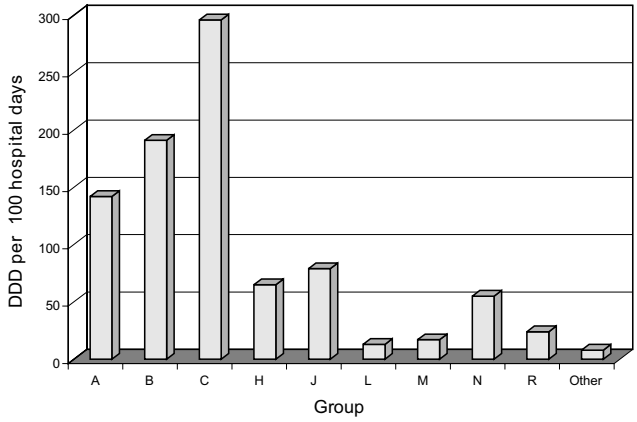

Fig. 3. Total drug consumption, expressed as defined daily doses (DDD) per 100 hospital days (Clinic of Internal Medicine, Dubrava University Hospital, Zagreb, Croatia, 2002): A – alimentary tract and metabolism, B – blood and blood forming organs, C – cardiovascular system, H – systemic hormonal preparations, J – antiinfectives for systemic use, L – antineoplastics and immunostimulating agents, M – musculo-sceletal system, N – nervous system, R – respiratory system, Other – other groups.

roid anti-inflamatory drugs (NSAIDs) was also observed (ketoprofen, diclofenac and indomethacin were simultaneously prescribed).

According to refs. 10 and 11, all potential drug interactions amounted to 356 or 7.2% of the total number of medication errors. According to more selective criteria of AHFS first (a), only 8 drug interactions or 2.3% of the 356 can be classified as clinically significant. Out of them 7 interactions were of severity level – 2 and one interaction of severity level – 3. The share of clinically significant interactions in the total number of medication errors amounted to 0.2% (Table I).

The incidence of medication errors in the entire sample, including all potential drug interactions, was 14.7%; one medication error occurred per each 6–7 prescriptions. How-

Table II. Share of hospitalized patients, number of prescriptions and medication errors according to age groups of patients

Age group (year)	Share of patients (%)	Share of prescriptions (%)	Share of medication errors (%)
20–30	2.2	0.9	0.1
31–40	4.3	3.1	1.2
41–50	20.6	18.1	2.4
51–60	21.5	24.3	25.6
61–70	31.3	34.6	38.6
71–78	20.1	19.1	32.1

ever, if only 8 interactions (out of 356 potentially possible interactions) were judged to be clinically significant, then the total number of all types of medication errors was 379. This resulted in an incidence of 7.7%, or one medication error per each 13 prescriptions (Table I). Certain types of prescribing medication errors significantly differed, as did the significance of those errors (Fig. 1).

The difference between the theoretically possible and clinically significant interactions is large and can be the cause of unnecessary over-interventions. Thus, a critical attitude is necessary when evaluating data on drug interactions. Use of relevant databases that enable rapid screening can greatly facilitate the daily practice of the clinical pharmacist in targeting interventions appropriately.

The problem of accurately estimating the incidence of drug interactions, particularly of distinguishing between clinically significant and non-significant, is well known. The results with regard to incidence differ, mainly because published studies have frequently used different criteria definition. Although the overall incidence of significant drug interactions is probably low (< 1%), it is still a considerable problem in terms of the global number of patients at risk and potential harmful consequences (12). Drug interactions can be pharmacokinetic or pharmacodynamic. Pharmacodynamic interactions are much less easy to predict and classify than those with a pharmacokinetic basis, which can be anticipated, though their extent is less easily predicted. Knowledge of drug interactions is an important parameter of rational pharmacotherapy.

The observed clinically significant interactions are shown in Table III. In all cases the prescribed therapy was corrected and/or the patients were more closely monitored.

Patients in the older age groups take more drugs simultaneously, which significantly increases the possibility of medication errors. The largest share of medication errors (38.6 %) was recorded in the group of patients aged from 61 to 70 years (Table II). Moreover, half of all observed clinically significant drug interactions were connected with the same group of patients. Elderly patients were the most endangered group of patients in that sense.

The results of this study concur with the literature data and indicate that systematic control of prescribed therapy is necessary. This is important because there is no serious publication about the existence of medication errors in Croatia. We began to carefully talk about it only a few years ago. Publication of medication errors would not have been possible 30 years ago anywhere in the world. There seemed to be a certain fatalism that medication errors were an inevitable by-product of patient care. No one had added up their number; no one had begun to categorize the types of errors; no one had recognized the immense learning and improvement opportunities. Medication errors were about the courage and intellectual curiosity of individuals who did not accept medication errors as inevitabilities and believed that improved systems and individual caregiver support could produce safer patient care.

Our findings point to the need of systematic control of prescribed therapies. This could be ensured by the application of the UDDDS in the hospital, because this system, contrary to the traditional floor stock system widely used in Croatian hospitals, directly involves clinical pharmacists in the medication process. Professional obligations of clinical pharmacists should include the control of prescribed therapy. The UDDDS, especially with computerized prescribing, would be justified in order to avoid medication er-

rors, both at the level of prescribing or administration (35, 36). It is imperative for pharmacists to cooperate with physicians, nurses and patients. Teamwork is fundamental to the effective medication error prevention system.

Table III. The observed clinically significant drug interactions

Observed interactions	Mechanism of interaction	Clinical effects	Action to be taken
DIGOXIN and PROPAFENONE (13, 14) severity level – 2	Mechanism is uncertain, but decreases in volume of distribution as well as renal and metabolic clearance of digoxin have been observed. Co-administration of these drugs may result in an increase in serum digoxin levels by 20–60%.	Increased digoxin level produces signs of toxicity: nausea, vomiting, ECG changes, (bradycardia, ventricular ectopy, QT interval shortening).	Propafenone should be used with caution in patients with serous structural heart disease. Serum digoxin levels should be monitored and patients should be observed for signs of digoxin toxicity and digoxin dosage should be adjusted.
DIGOXIN and AMIODARONE (15, 16) severity level – 2	Multiple mechanisms appear to be involved. Amiodarone decreases renal and nonrenal clearance of digitalis glycoside, reduces the volume of distribution and increases digoxin bioavailability.	Increased digoxin level depresses the sinus node, resulting in bradycardia, and produces other signs of toxicity. Magnitude of the interaction is proportional to the amiodarone dose and serum level.	Serum digoxin levels should be monitored and patients should be observed for symptoms of digoxin toxicity and the dosage should be adjusted accordingly.
DIGOXIN and VERAPAMIL (16–18) severity level – 2	Verapamil may reduce the clearance of digoxin and may displace digoxin from its tissue binding sites. Co-administration may result in an increase in digoxin serum levels by 50.70%.	Increased digoxin level produces signs of toxicity. Possible predisposing factors include hepatic impairment, older age and low heart rate.	Serum digoxin level should be monitored and patients should be observed for symptoms of toxicity and the dosage should be adjusted accordingly. Increased concentrations may occur within seven days of therapy initiation.
THEOPHYLLINE and ALLOPURINOL (20–23) severity level – 2	Allopurinil may inhibit the metabolism of theophylline, increasing its serum level.	Increased theophylline serum levels may result in theophylline toxicity.	Serum theophylline levels should be monitored and the dosage may need to be decreased.

Table III. continued

Observed interactions	Mechanism of interaction	Clinical effects	Action to be taken
AMIODARONE and WARFARIN (24-27) severity level – 2	Amiodarone may inhibit the metabolism of warfarin by cytochrome P450, increasing its serum level.	Increased warfarin serum levels may result in an increase in the clinical effects of the anticoagulant and an increased risk of bleeding.	Prothrombin activity should be carefully monitored and the dose of warfarin should be adjusted as needed. Some researchers recommend reducing the initial anticogulant dose by 25 to 50%. It may take several weeks of concurrent therapy before the full effect of this interaction is seen.
GENTAMICIN and FUROPSEMIDE (28, 29) severity level – 2	Mechanism of action is additive or synergistic ototoxicity.	Rapid onset of ototoxicity may be observed with possible severe or permanent hearing loss.	Hearing function should be monitored. High dosages, paricularly in patients with impaired renal function should be avoided. This interaction is likely to occur, although clinical documentation is limited.
KETOCONAZOLE and RANITIDIN (30, 31) severity level – 2	Ranitidin increases the stomach pH, reducing dissolution and gastrointestinal absorption of the azole antifungal.	Clinical effectiveness of the antifungal may be reduced.	Concurrent administration of ranitidine and cimetidine with azole antifungal drugs should be avoided. An interaction can be expected to occur with other H-2 antagonists.
HYDROCHLOROTIAZID + AMILORIDE and DICLOFENAC (32–34) severity level – 3	The exact mechanism is unknown. However, NSAID inhibition of prostaglandins production may allow amiloride or triamterene induced nephrotoxicity or hyperkalemia to occur.	Renal failure or hyperkalemia is possible.	Concurrent therapy of these drugs, including other NSAIDs, should be avoided. If these drugs are used concurrently, renal function and serum electrolytes should be monitored.

2 – severe interaction, 3 – moderate interaction

CONCLUSIONS

The difference between the incidence of theoretically possible and clinically significant drug interactions is quite large (7.2 *vs*. 0.2%) and can be the cause of unnecessary over-interventions. Thus, a critical attitude is necessary when evaluating the data on

drug interactions. Use of relevant databases that enable rapid screening can greatly facilitate the daily practice of the clinical pharmacist.

Our findings point to the need of systematic control of prescribed therapies which could be ensured by the application of the UDDDS in the hospital.

A painful method of error prevention is to learn from previous errors. It is important to take into account the potential risks of future errors, as well as to acquire information on errors that have previously occurred. A medication errors reporting program should be established, both at the hospital and national levels in Croatia, enabling systematic data collection and sharing the information about medication errors in order to prevent and reduce their incidence in the future.

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S A Ž E T A K

Propisivačke medikacijske pogreške za hospitalizirane bolesnike: Prospektivna studija

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Svrha ove prospektivne studije je ispitivanje pojavnosti i vrsta medikacijskih pogrešaka u propisivanju i prevenciji njihovog nastanka. Podaci ispitivanja odnose se na 4951 propisani lijek, u razdoblju od 25 tjedana 2002. godine. Ispitivane medikacijske pogreške definirane su kao: pogrešna doza, pogrešan interval doziranja, dupliciranje terapije, te interakcija lijekova. Pojavnost medikacijskih pogrešaka propisivanja na ispitivanom uzorku, uključujući sve teoretski moguće interakcije lijekova, iznosila je 14.7%. Međutim, kako je samo 8 interakcija (od ukupno 356 teoretski mogućih) ocijenjeno klinički značajnim, ukupan broj medikacijskih pogrešaka iznosio je 379 (od 4951 zapisa), što odgovara pojavnosti od 7.7%. Pogreška doziranja lijeka bila je najčešća vrsta uočenih medikacijskih pogrešaka. Utvrđena je velika razlika između incidencije teoretski mogućih i klinički značajnih interakcija lijekova (7.2 *vs*. 0.2%). Nužan je kritički pristup procjeni dostupnih podataka vezanih za interakcije lijekova. Rezultati našeg istraživanja upućuju na nužnost sustavnog nadzora propisane terapije, koji bi se mogao osigurati primjenom sustava raspodjele jedinične terapije. U Hrvatskoj bi se trebao uspostaviti program praćenja medikacijskih pogrešaka, kako u bolnicama tako i na nacionalnoj razini.

Ključne riječi: interakcije lijekova, medikacijske pogreške, propisivanje lijekova, prospektivna studija

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