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A medication database – a tool for detecting drug interactions in hospital

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Abstract *Objective*: Drug interactions may lead to life-threatening injuries. More often, however, they lead to slow recovery, induce slight symptoms or result only in potential injury. Therefore, clinicians are not always aware of using potentially interacting drug combinations. An on-line alarming system of potential drug interactions was developed in Turku University Central Hospital. In the present study, we utilised the system to find out the incidence and nature of potential drug interactions occurring in a representative hospital patient population.
Methods: Computerised anatomical therapeutic chemical (ATC)-coded patient medication data of 2547 patients, treated in two internal medicine wards, were combined with an ATC-coded rule base of drug interactions. All potential drug interactions in the study population were searched for.
Results: A total of 326 potentially serious drug interactions were detected in the study population. The number of patients in this group was 173, i.e. 6.8% of all patients had one or several drug combinations which might have led to serious clinical consequences. Concomitant use of calcium and fluoroquinolones (decreased absorption) was the most common mistake (66 prescriptions).
Conclusions: Potentially inappropriate drug combinations seem to occur frequently. Structured and coded medication data can be utilised efficiently to detect potential drug interactions in hospital. Computerised on-line monitoring and automatic alarming of potentially hazardous drug combinations might help clinicians to prescribe more safely, but further development of the system is needed to avoid unnecessary alarms.

Key words Drug Interactions, Hospital

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Introduction

A substantial part of medical treatments lead to injuries [1]. The most common reason (19.4%) for these injuries is drug complications [2], which are often due to errors in the use of drugs [3]. According to previous studies, medication errors occur in 2–14% of patients admitted to hospitals [4, 5], but fortunately, most do not result in injury [6, 7]. However, the goal should be that no errors reach the patient [8]. Computerised approaches are ideal for this because reliability can approach 100%, while methods that rely on human inspection will always miss some errors [3].

According to Bates et al., the leading causes of medication errors – drug interactions, negligence of known allergies, overdoses, underdoses, wrong choices and wrong medication frequencies – were found to be potentially preventable by computerised order checking [3]. In Turku University Central Hospital (TUCH), an integrated computerised system with a structured medication database was introduced to detect and avoid medication errors. Our interest focuses on warning of drug interactions and known allergies as well as drug effects on laboratory tests.

Cumulative individual patient medication data are stored continuously in an ATC-coded medication database. The structured form of the medication database enables us to process and utilise the medication data in several applications [9]. The medication database can be combined with structured knowledge and rule bases, which makes automatic alarming of errors possible. We already have a structured knowledge base for drug interactions [10] and we are building one for drug effects

tinuing a certain medication. If someone intends to start the same medication again, the system will automatically display the earlier reason for discontinuation, for example an allergic reaction.

Drug interactions are typical examples of medication errors that may lead to serious injuries [12], but are potentially preventable by computer systems [3]. In our system, the interaction database is integrated into the medication database for continuous monitoring of the current medication profiles of individual patients. Online alarms of potential drug interactions can be produced directly to clinicians on the wards. To evaluate the system and to find out the incidence and nature of potential drug interactions occurring in a hospital patient population, a retrospective study utilising the combined medication and interaction databases was performed.

Subjects and methods

Study population

A total of 2547 patients were included in the study. The study population consisted of patients treated in two internal medicine wards of the TUCH. The two study wards were the nephrological (595 patients) and the cardiological units (1952 patients). The individual medication data of all patients in these units were managed by the computerised system. The nephrological unit had used the system for 13 months and the cardiological unit for 7 months. These periods determined the respective periods of gathering the data. In the study wards, automatic alarms of drug interactions were not used and the wards were not aware of the study.

The study wards are representative examples of great drug consumers in hospital and, therefore, drug interactions are likely. In the nephrological unit, drug treatments are far more complicated than in most other departments. The most difficult cases of hypertension, complications of autoimmune diseases or diabetes, as well as severe infections in immunocompromised patients are quite common. The cardiological unit covers the most usual diagnoses in internal medicine and in earlier studies [13], cardiovascular drugs were found to be represented in the majority of potential drug interactions.

Medication database and coding of medication data

The medication data of individual patients were stored in the medication database, in which the trade names of drugs were converted into their respective anatomical therapeutic chemical (ATC) codes. The ATC code [14] was used for coding drugs also in the interaction database. The basic data structure in the medication database is called a medication line. The information in each line consists of nine fields: (1) social security number (identification) of the patient; (2) ward; (3) trade name and strength of the drug; (4) pharmaceutical form of the drug; (5) dose of the drug; (6) ATC code of the drug; (7) date of onset of the medication; (8) date of stopping the medication; and (9) reason for stopping the medication, if required. Typically, one patient has several medication lines.

Interaction database

The data on drug interactions were based on FASS (Farmakologiska Specialiteter i Sverige) 1995 [10]. FASS is the Swedish physician's desk reference containing all registered drugs in Sweden. It includes a comprehensive chapter on drug interactions between drug groups and all of them are classified according to the clinical importance and level of scientific documentation. The clinical importance of the interaction is coded with letters from A to D. Letter A corresponds to "probably no clinical importance", B to "clinical importance not yet confirmed", C to "combinations which may require a modified drug dosage schedule" and D to "interactions which may result in serious clinical consequences". The level of scientific documentation is coded with numbers from 1 to 4. Number 1 refers to "incomplete case reports", 2 to "well-documented case reports", 3 to "studies with healthy volunteers" and 4 to "controlled studies of the relevant patient material". For each interaction, the catalogue includes a comment on the nature of interaction and, if possible, short instructions on how to avoid the interaction. Our interaction database was built on the basis of the FASS data.

Combining the medication database with the interaction database

All drug treatments stored in the medication database at the study wards during the study periods were analysed. The interaction database, including the ATC codes of the interacting drug combinations listed in FASS 1995, was used to find out "forbidden" combinations in the medication database. As a result, we obtained a list of all potential drug interactions in the study population. The list included trade names, forms, doses and ATC codes of the interacting drugs, social security numbers and wards of the patients, dates of starting and stopping the medication as well as clinical importance and level of documentation of the detected interactions.

Results

A total of 22 508 prescriptions were stored in the medication database in the study wards during the follow-up periods (7 and 13 months). The drugs most commonly prescribed in the study wards are listed in Table 1. The number of patients receiving two or more drugs concurrently was 2347.

Potentially serious interactions, i.e. interactions belonging to FASS group D, occurred in 326 prescriptions out of 22 508 (1.4%). The number of patients in this

Table 1 Drugs most commonly prescribed in study wards

Drug or drug group	Number of prescriptions
Diuretics	1852
Antibiotics	1818
β-Adrenoceptor blockers	1403
Long-acting nitrates	1370
Calcium channel blockers	1145
Acetylsalicylic acid	1121
Hypnotics and sedatives	1077
Antidiabetic therapy	814
Antiepileptics	812
Corticosteroids for systemic use	777
ACE inhibitors	761
Peptic ulcer therapy	679
Digoxin	567
Dipyridamole	523
Nonsteroidal anti-inflammatory drugs	497
Calcium salts	469
Potassium salts	427
Oral anticoagulants	373
Laxatives	308

group was 173. This means that 6.8% of all patients and 7.4% of patients taking two or more concurrent drugs had one or several drug combinations which might have led to serious clinical consequences and, therefore, ought to have been avoided. Most of these combinations were potentially hazardous due to increased toxicity and the rest of them were potentially ineffective due to decreased absorption of either drug. Potentially toxic drug combinations occurred in 222 prescriptions (1.0%) covering 121 patients (4.8%). Potentially ineffective drug combinations due to decreased absorption occurred in 104 prescriptions (0.5%), covering 56 patients (2.2%). Four patients (0.2%) had both potentially toxic and ineffective drug combinations. If we classify these 326 "group D interactions" according to the level of documentation by FASS, 54 interactions belonged to class 4, 239 to class 3, 15 to class 2 and 18 to class 1. Consequently, 89.9% of the potentially serious interactions detected by the system belonged to FASS documentation class 3 ("healthy volunteers") or 4 ("relevant patient material") and can be considered to be well documented. Furthermore, 1460 (57.3%) patients were exposed to interactions classified under groups C, B and A, but these prescriptions were not scrutinised further because of their minor clinical importance.

The ten most frequent potentially serious interactions between drugs or drug groups and the nature of interactions are listed in Table 2. These top ten interactions, 286 in total, correspond to 87.7% of all potentially serious interactions detected.

Discussion

Prescribing potentially inappropriate drug combinations was relatively common in our hospital. Potentially serious drug interactions occurred in 1.4% of the prescriptions and in 7.4% of the patients taking two or more drugs concurrently. Seventy per cent of these patients had potentially toxic drug combinations and 32% had potentially ineffective combinations due to decreased absorption of either drug. Furthermore, in our study population, 57.3% of the patients were exposed to potential interactions of minor clinical importance.

According to Linnarsson's study [13] in primary health care, potential drug interactions occurred in 12% of patients receiving two or more concurrent drugs and 1.9% of all prescriptions resulted in a potential drug interaction. In a study by Dambro and Kallgren [15] in a family practice, 9.2% of the study patients were prescribed drugs with known interaction potential. Seventeen per cent of these potential interactions were considered to be of "major" clinical significance. In both studies, the concurrence of potentially interacting drugs was estimated from overlapping prescriptions, while in our study, the concurrence was determined by the exact dates of starting and stopping the medications. The differences between study populations in hospital and primary health care may also have had an impact on the incidence of potential drug interactions. In an overview of drug interaction screening, Jankel and Speedie [16] have evaluated 19 studies aiming at measuring the frequency of drug interactions. The incidence of all potential drug interactions varied from 2.2% to 70.3%. Differences in study designs, methodologies, populations and definitions have probably again contributed to the considerable variation in the reported incidence rates.

Our study was carried out in a hospital setting in two internal medicine wards. Here, the clinicians are experts in drug treatments and, therefore, complications of drug treatments should be quite rare. In primary health care, the incidence of potential drug interactions can be anticipated to be higher because a wider range of drugs is used by general practitioners than hospital specialists, who are often experts in certain drug treatments. In

Table 2 The ten most frequent potentially serious drug interactions, number of prescriptions and nature of interaction

Drug(s)	Drug(s)	Number	Nature of interaction
Calcium salts	Fluoroquinolones	66	Calcium inhibits the absorption of fluoroquinolones
Potassium salts	Spironolactone	54	Risk for hyperkalaemia
Verapamil	β-Adrenoceptor blockers	38	Risk for bradycardia
Warfarin	Acetylsalicylic acid	27	Potentiation of anticoagulation, inhibition of thrombocyte function
Warfarin	Amiodarone	23	Amiodarone inhibits the metabolism of warfarin
Warfarin	Nonsteroidal anti-inflammatory drugs	23	Risk for gastrointestinal bleeding due to inhibition of platelet aggregation and damage of the gastrointestinal epithelium
Iron	Fluoroquinolones	20	Iron inhibits the absorption of fluoroquinolones
Sucralfate	Fluoroquinolones	16	Sucralfate reduces the absorption of fluoroquinolones
Morphine	Barbiturates	10	Enhanced depressive effect on respiration
Diltiazem	Nifedipine	9	Diltiazem decreases the clearance

hospital, colleagues may also check each other's prescriptions. Obviously, the use of potentially inappropriate drug combinations is sometimes unavoidable. When we scrutinised the 286 potential drug interactions listed in Table 2, it turned out that many of the detected "forbidden" drug combinations, for example spironolactone and potassium chloride as well as verapamil and beta-adrenoceptor blockers, were used deliberately. The risk of interaction was considered and the doses of drugs in question were adjusted to be safe and effective. In these cases, specialists may find automatic interaction alarms unnecessary and frustrating, but the same alarms are probably of great educational importance for junior doctors.

Although potentially serious drug interactions are relatively frequent, they seldom lead to serious injuries [15, 17]. However, the resulting injuries may be devastating [12] while often preventable by computer systems [3]. We believe that hints of potentially inappropriate drug combinations should help clinicians to prescribe more safely. In our system, on-line alarms of potentially serious drug interactions can be produced directly to clinicians in the wards. The system automatically checks for all potential drug interactions in the current patient medication profiles, not only those suspected by the clinicians. This automation is an important aspect, because computer-based tools that require additional efforts, beyond the usual routine, do not easily gain wide acceptance among clinicians [18, 19].

Computers are supposed to provide information needed to prescribe safely [20]. As for drug interactions, the type of interaction is of particular importance. Therefore, the type of interaction and short instructions how to avoid the interaction are included in the alarm given to clinicians, as soon as the medication is stored in the medication database, i.e. before the medication is given to the patient. Also, the pharmaceutical form of the drug plays a major role in drug interactions. If, for example, either of the "interacting" drugs is given parenterally, it is unnecessary to warn about decreased absorption of either drug. In these cases, the nature of interaction can be seen in the instruction mentioned above, but we should devise a better strategy to avoid this problem of "false alarms". Unfortunately, the ATC code does not differentiate between parenteral and peroral dosage of drugs.

Overall, the ATC coding for drugs appeared to function very well. The hierarchical structure of the ATC code is practical in our application, because often a whole group of drugs interacts with certain drugs. The group, for example beta adrenoceptor blockers, can be defined with one single ATC code in the interaction database but can still be found in the medication database as individual beta blockers. The only major error in the detected potential drug interactions was the combination of sodium bicarbonate and ciprofloxacin. The reason for this "false alarm" was the fact that, according to our interaction database, antacids interact with fluoroquinolones and calcium interact with fluoroquinolones [21–23]. Therefore, in this case, the individual ATC codes for antacids containing Mg, Al and Ca should be fed into the rule base, instead of the whole group of antacids. Neither type of "false alarms" mentioned above was included in the reported incidence rates of potential drug interactions.

ATC coding was one of the main reasons for choosing the FASS as the source of interaction data. Another important aspect was the classification used in the FASS. It offers an ability to limit the drug interaction screen to a certain level of clinical significance and documentation. However, the final classification of seriousness of the potential interaction remains, in all cases, a clinician's personal opinion and will, above all, vary with the clinical situation.

The structuring and coding of data in our system is the basis for the functioning of the system. Once the ATC-coded medication database is built, it can be used to avoid medication errors in several connections. Apart from drug interactions, overdoses and underdoses could be detected. As mentioned earlier, our system already monitors known allergies. We are also planning to build an alarming system for drug effects on laboratory tests [11]. Furthermore, clinical practice can be monitored effectively. For instance, it is possible to check how guidelines for treating patients with hypercholesterolaemia or hypertension are followed. This kind of monitoring helps us to identify the actual problems in medication, facilitates quality assurance and enables drug utilisation research, which is becoming an important tool in health economics.

Even if computers can never replace clinical judgement, computer-based tools assist prescribing in various ways [19]. However, there is a lack of studies establishing the real benefits brought about by these systems. In this study, we have shown how detailed information about clinical practice can be easily obtained by means of a computerised hospital information system and discussed how this system can be utilised to avoid errors in drug treatments. In the near future, our aim is to perform a prospective study to evaluate, objectively, the impact of our alarming system on the quality and costs of patient care.

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