

Identification of potential drug-related problems in the elderly: the role of the community pharmacist

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Abstract *Objective:* The high prevalence of multiple drug use combined with age-related changes in pharmacokinetics and pharmacodynamics makes older adults more vulnerable to drug-related problems (DRPs). This pharmacy-based study was performed to identify potential DRPs from prescription records of the elderly and the role of the pharmacist in this process. *Method:* The study was performed from June 2002 to February 2003 in 16 community pharmacies in the Netherlands. Medication assessment of elderly patients aged 65 and over using six or more drugs concomitantly took place on the date of inclusion. Ten types of potential DRPs, grouped into three categories, were determined. The three groups were patient-related, prescriber-related or drug-related potential DRPs. We looked at the occurrence, nature and determinants of differential potential DRPs. *Results:* The mean number of prescriptions per patient was 8.7. In total 3.9 potential DRPs per elderly person were identified. The distribution of the potential DRPs over the three categories was: patient related 4.7%, prescriber related 55.7% and drug related 39.6%. Use of

NSAIDs (OR 29.9; 95% CI 4.1–219) and digoxin (OR 15.7; 95% CI 4.9–50.5) were associated with the highest risk for potential DRPs. *Conclusion:* In this vulnerable group of elderly patients potential DRPs frequently occur. Community pharmacists can play an important role in the identification, assessment and prevention of potential DRPs in the elderly. It is useful to investigate which part of potential DRPs can be avoided by the intervention of the community pharmacist in collaboration with the prescriber and the patient.

Keywords Drug-related problems · Polypharmacy · Multiple drug use · Elderly · Medication assessment · Community pharmacists · The Netherlands

Introduction

In 2003, 13.7% of the total population in the Netherlands was over 65 years of age and the proportion of older adults is forecasted to increase to 18.2% in 2020. Elderly people are using more medications than younger people [1]; the use of drugs in elderly patients is almost higher by a factor of three compared to the non-elderly population. The prevalence of polypharmacy in Dutch elderly patients (65 or older), when defined as the concurrent use of two or more medications, is approximately 30% [2].

The more frequent use of drugs by the elderly can be explained by the high prevalence of multiple morbidity and the increased availability of pharmacotherapeutic options during recent decennia. In addition, the increasing adoption of the concept of evidence-based medicine could have contributed to polypharmacy, because new drugs are usually studied as an addition to a cocktail of drugs that until then had proven to be the best treatment [3]. Medication use (including polypharmacy) can certainly improve quantity and

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quality of life. The shadow side of multiple drug use, however, is the frequent occurrence of different drug-related problems (DRPs) such as adverse drug reactions, drug–drug interactions, contraindications and underutilisation [4]. The elderly are more prone to such DRPs not only because of the higher prevalence of drug use and morbidity but also due to ageing related pathophysiologic changes leading to altered pharmacokinetics and pharmacodynamics making them more susceptible to the (adverse) effects of drugs [5, 6].

Another complicating factor is that prescriptions for one patient are often initiated by more than one doctor (polyprescribing) hampering an adequate overall pharmacotherapeutic overview and treatment plan. The prescription cascade (initiation of medication to treat symptoms that are in fact unrecognised adverse drug reactions of the use of another drug) is a possible consequence of this [7].

In various studies evaluating multiple drug use in the elderly, the increased risk for DRPs has been shown [8–12]. Different coding systems in practice for documentation of these DRPs [13–15], more or less comprehensive and mostly not easy to apply in daily practice.

In the Netherlands there is a high patient–pharmacy registration, so it seems an ideal situation and opportunity for community pharmacists to be involved in the identification of potential DRPs. In accordance with the standard system of medication surveillance, a pharmacy-based study was initiated with the objective to identify potential DRPs from prescription records, encountered in people aged ≥ 65 using six or more drugs concomitantly.

Methods

Setting and study population

The study was performed from June 2002 to February 2003 in 16 community pharmacies located in the southern part of the Netherlands. The participating pharmacies were collaborating with a research group to perform pharmacy practice research. Each participating pharmacy randomly selected from its prescription registration database up to 20 patients aged 65 and over, taking six or more prescription medications on a certain date during the study period (=date of inclusion). Patients living in nursing homes and those hospitalised in the year preceding the date of inclusion were excluded.

For a proper assessment of potential DRPs, reasons for prescribing all the medications used on the date of inclusion were obtained from the medical record of the general practitioner (GP). Patients were excluded, if the GP was either unable or unwilling to cooperate.

Assessment of potential DRPs

For each patient a drug use profile was printed listing all prescribed drugs, dispensed for that patient during the year preceding the date of inclusion. Potential DRPs were assessed by the patient's pharmacist for all medications used on the date of inclusion and documented on a standardised report form. Drugs were classified according to the Anatomical Therapeutic Chemical coding system. In several research meetings, the participating pharmacists were trained about classifying and documenting the potential DRPs. DRPs were identified and judged in agreement with national prescribing guidelines such as the Standards for Dutch general practitioners and therapeutic handbooks [16, 17] but also left room for the professional interpretation by the individual pharmacist. During the study period the principal investigator (T.H.A.M.V.) was available for consultation. Finally, all data with the identification of potential DRPs by the individual pharmacist were reviewed and when necessary adjusted by the principal investigator (T.H.A.M.V.). The nature of predefined mutually exclusive potential DRPs grouped to three categories were identified, namely:

1. *patient-related potential DRPs*: non-compliance;
2. *prescriber-related potential DRPs*: no longer existing indication, therapeutic duplication, inappropriate dosage (over and underdosage), off label use, undertreatment, inconvenience of use; and
3. *drug-related potential DRPs*: contraindication, drug–drug interaction, drug treatment of adverse drug reaction.

Non-compliance was defined as the occurrence of two or more gaps of 20 days between the dispensing date and the theoretical end date of the prior dispensing of the same drug during the year preceding the date of inclusion. No longer existing indication was defined if the indication for a certain prescription was disputable or not evidence-based anymore. Therapeutic duplication was defined as the use of two or more drugs with the same ATC-code in the fifth level e.g. flurazepam (ATC-code N05CD01) and temazepam (ATC-code N05CD07) or with similar pharmacodynamic properties (e.g. oxazepam and temazepam). Undertreatment was defined in cases where there was no prescription for an actual indication according to national guidelines (e.g. an indication exists, but no drug is prescribed such as, no prescription of a bisphosphonate in case of long-term use of an oral corticosteroid). Inconvenience of use was defined as the opportunity to simplify the drug regimen e.g. by choosing a different formulation making a once daily instead of a thrice daily regimen possible or by choosing a fixed drug combination instead of two separate preparations.

Drug treatment of an adverse drug reaction was for example the use of a laxative with concomitant use of verapamil (constipation caused by verapamil).

Inappropriate dosage, off label use, contraindication and drug–drug interactions were estimated according to national textbooks [16, 17].

Data analysis

The occurrence of potential DRPs was calculated by dividing the total number of encountered potential DRPs by the number of patients. To determine whether specific medication groups were relatively more frequently associated with potential DRPs than others, a case–control analysis was performed. In that analysis medications with a potential DRP were considered as cases and medications without a potential DRP were taken as controls. The strength of the association between a given medication group and potential DRPs was expressed as odds ratios (OR) with corresponding 95% confidence intervals (95% CI). In this calculation more than one potential DRP could be associated with one particular prescribed medication. So for interactions and (pseudo)double medication, where more than one drug is involved, potential DRPs were counted for each involved medication. On the contrary, each different interaction and (pseudo)double medication were counted once per patient. Data management was performed with Microsoft Access and statistical analysis with SPSS version 11.0.

Results

In total 196 elderly patients (54 males, 142 females) were included in this study. The mean (SD) age was 77.0 (6.4) years. The mean (SD) number of drugs used on the date of inclusion was 8.7 (2.5) and varied from 6 to 18. Antithrombotics, diuretics, antilipaemics, beta-blockers, nitrates and oral antidiabetics were the six most frequently prescribed medications (Table 1).

A total of 763 potential DRPs were observed in the 196 patients, which corresponds to 3.9 potential DRPs per elderly person. Two or more potential DRPs occurred in 90% of the included patients and in almost one third of the study population five or more potential DRPs were identified. The most frequently occurring potential DRPs were no longer existing indication (23.7%), contraindication (20.7%), drug–drug interactions (17.8%) and inconvenience of use (11.7%) (Table 2). With respect to grouping of DRPs into the three categories the distribution of the potential DRPs was: patient related 4.7%, prescriber related 55.7% and drug related 39.6 (Table 2).

Use of NSAIDs (OR 29.9; 95% CI 4.1–219), digoxin (OR 15.7; 95% CI 4.9–50.5), hydrokinine

Table 1 Most frequently prescribed medication groups

Medication group (ATC)	Number ^a	%	Number ^b	%
Antithrombotics (B01A)	156	9.2	143	73.0
Diuretics (C03A, C03B, C03C)	104	6.1	103	52.6
Antilipaemics (C10A)	91	5.4	85	43.4
Betablockers (C07A)	90	5.3	88	44.9
Nitrates (C01D)	89	5.2	68	34.7
Oral antidiabetics (A10B)	89	5.2	62	31.6
Inhalation therapy (excl. β -sympathomimetics) (R03B)	65	3.8	44	22.4
ACE-inhibitors (C09A)	64	3.8	64	32.6
H2-receptor antagonists/proton-pump inhibitors (A02B)	63	3.7	63	32.1
Insulin (A10A)	55	3.2	39	19.9
Total	866	50.9		

^aNumber of prescriptions (R_x) [total number: 1700]. ^bNumber of elderly patients [total number: 196].

(OR 4.1; 95% CI 1.2–14.4), verapamil/diltiazem (OR 3.8; 95% CI 1.4–10.2), diuretics (OR 3.1; 95% CI 2.0–4.6) and betablockers (OR 2.7; 95% CI 1.8–4.1) was associated with the highest risk for potential DRPs (Table 3).

The association between categories of potential DRPs and medications with the highest risk for potential DRPs is shown in Fig. 1. Most of the potential DRPs were drug related, except hydrokinine in which the potential DRPs were predominantly prescriber related.

Discussion

We found that in this vulnerable group of older adults using six or more drugs concomitantly, potential DRPs frequently occur. The nature of these DRPs was mainly prescriber-related DRPs (especially no longer

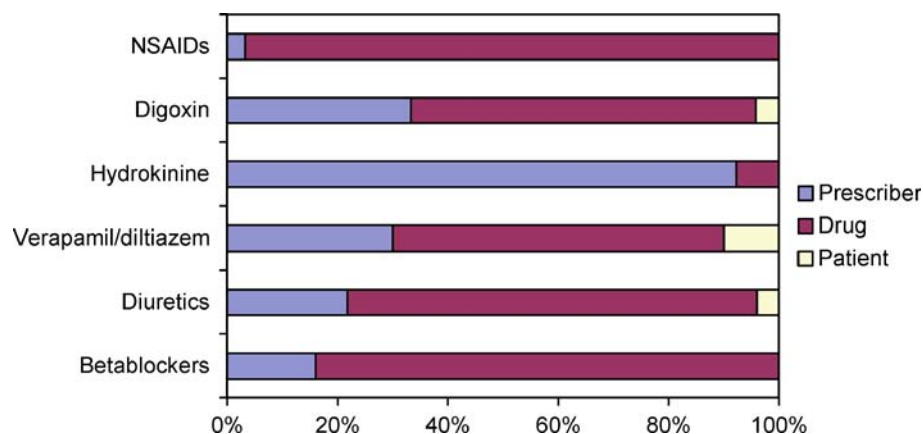
Table 2 Nature of the encountered potential DRPs

	Frequency	%
Patient related	36	4.7
Non-compliance	36	4.7
Prescriber related	425	55.7
No longer existing indication	181	23.7
Therapeutic duplication	71	9.3
Inappropriate dosage	69	9.0
Off label use	7	0.9
Undertreatment	8	1.0
Inconvenience of use	89	11.7
Drug related	302	39.6
Contraindication	158	20.7
Drug–drug interaction	136	17.8
Drug treatment of adverse drug reaction	8	1.0
Total	763	100.0

Table 3 Medication groups with the highest risk for potential DRPs

Medication group (ATC)	DRPs ^a		No DRPs ^b		OR	95% CI
	<i>n</i>	%	<i>n</i>	%		
NSAIDs (M01A)	31	3.20	1	0.11	29.9	4.1–219
Digoxin (C01A)	48	4.95	3	0.33	15.7	4.9–50.5
Hydrokinine (M09A)	13	1.34	3	0.33	4.1	1.2–14.4
Verapamil/diltiazem (C08D)	20	2.06	5	0.55	3.8	1.4–10.2
Diuretics (C03A, C03B, C03C)	101	10.42	33	3.65	3.1	2.0–4.6
Betablockers (C07A)	87	8.98	32	3.54	2.7	1.8–4.1

^aTotal of DRPs (cases): 969 (100%). ^bTotal of no DRPs (controls): 905 (100%)

Fig. 1 Nature of the potential DRPs for medication groups (ATC) associated with the highest risk for potential DRPs

existing indication) and drug-related (e.g. drug–drug interactions and contraindications). In addition, we found that the use of several specific medications (e.g. digoxin, NSAIDs) was associated with a high risk for potential DRPs.

However, there are potential limitations to our study. First, we assessed potential DRPs instead of actual DRPs meaning that we did not study whether the patients with potential DRPs also had worse clinical outcomes during follow-up. Potential DRPs are generally considered to be a good proxy for actual DRPs, although good validation studies still have to be conducted [18].

Second, registration of non-prescription drugs such as laxatives and NSAIDs is not complete in Dutch pharmacies. Patients may also obtain these drugs from non-pharmacy outlets (e.g. chemist). This can possibly cause an underestimation of potential DRPs.

Third, we excluded the patients of GPs unable or unwilling to cooperate because for a good identification of potential DRPs, the data from the medical record of the GP are required. Probably this will result in an underestimation of the occurrence of potential problems because it is conceivable that the cooperating GPs themselves were more aware of appropriate prescribing.

Fourth, the problem of non-compliance could be underestimated, because we determine non-compliance from dispensing data, not actually knowing if the dispensing drugs were really taken.

Fifth, the training of the participating pharmacists could be insufficient. Therefore all data were reviewed and when necessary adjusted by the principal investigator.

Finally, this study involved elderly patients aged 65 or over using six or more drugs concomitantly. The findings may not be generalised to the whole group of elderly.

Direct comparison of our findings with those from other studies is difficult as there is a wide variety in populations studied and methods used for the identification and classification of DRPs.

Beers et al. [19, 20] developed the first set of explicit criteria to measure inappropriateness of drugs, which were updated in 1997. Using these explicit criteria Zhan et al. [21] reported that one in five elderly patients receives an inappropriate drug or dosage. Another assessment for drug therapy appropriateness is the Medication Appropriateness Index (MAI) [22, 23]. Knight et al. [24] developed 12 quality indicators for appropriate medication use in elderly patients. Recently, Sorensen et al. [25] discussed a coding system for assessment of the appropriateness of pharmacists' medication reviews. However, there is still no gold standard available for assessment of appropriateness of medication use. All these instruments can be considered as tools to improve the quality of medication use in the elderly, and each has its pros and cons. Coding systems are important tools for the documen-

Table 4 The role of the community pharmacist in the identification, evaluation and prevention of potential DRPs in the dispensing process

Potential DRP	Identification by ^a	Intervention moment ^b	Intervention to
Patient related			
Non-compliance	MR	> 2	Patient
Prescriber related			
No longer existing indication	MR	> 1	Prescriber
Therapeutic duplication	MSS	1	Prescriber
Inappropriate dosage	MSS	1	Prescriber
Off label use	MR (Handbooks)	> 1	Prescriber
Undertreatment	MR (Guidelines)	> 1	Prescriber
Inconvenience of use	MR	> 1	Patient/Prescriber
Drug related			
Contraindication	MSS	1	Patient/Prescriber
Drug–drug interaction	MSS	1	Patient/Prescriber
Drug treatment of adverse drug reaction	MR	1	Prescriber

^aMR: Medication Review by the community pharmacist; MSS: Medication Surveillance Signals by the Pharmacy Information System. ^b1: at the moment of the first prescription; > 1: after more than one prescription; > 2: after more than two prescriptions

tation of DRPs. Meyboom et al. [26] noticed that a uniform classification of DRPs suitable for daily practice is not easily available. In the literature a variety of coding systems is available [13, 14]. They should be suitable not only for scientific studies. A suitable coding system must be easy to use in daily routine and facilitated to computer aided use. That's why we used a "tailor made" classification system according to own practice and not a derivation of an already existing classification system. This approach can be considered as practical and suitable, in line with and complementary to the standard practise of (automated) medication surveillance in Dutch pharmacies.

In line with other studies is our finding that in the elderly DRPs frequently occur with NSAIDs [27–29]. This can be explained by the high potential of these drugs for drug–drug interactions (e.g. beta blockers, loopdiuretics, ACE-inhibitors), contraindications (e.g. heart failure) and side effects (e.g. gastrointestinal).

Intervention by the pharmacist can significantly improve appropriate prescribing in elderly patients with polypharmacy [30, 31]. No longer existing indication as the most occurring potential DRP in our study supports the opportunity to discontinue a certain drug by reevaluating the original reason for prescribing that drug through consultation with the prescriber. Inconvenience of use, in our study a frequently occurring DRP, has not often been a subject of assessment in other studies. Simplifying the often complex drug regimens in the elderly can easily be done resulting in a practical benefit for the individual patient and possibly improve adherence [32, 33]. In this study the role of the community pharmacist has been focussed on identification of potential DRPs in elderly patients. The logical

next step is to evaluate and to prevent these potential DRPs. Table 4 shows the types of DRPs, the possible tools for identification, the persons whom the pharmacist can intervene and the timing of intervention within the dispensing process of the drugs. Medication review and medication surveillance signals of the Pharmacy Information System are currently the most important tools for identifying potential DRPs. The penetration of knowledge systems into medical practice will certainly further improve automated identification of potential DRPs in future, especially those signals that can only be identified after prolonged use of the drug, such as non-compliance.

If the pharmacist proclaims a role in the assessment of DRPs it seems better to focus on the identification, evaluation and prevention of patient- and prescriber-related problems because these problems seem more likely to successful interventions by the community pharmacist than drug-related DRPs are. Patient-related DRPs as well as prescriber-related DRPs depends in some degree on human factors, like for instance: knowledge, education, attitude and awareness. Drug-related DRPs on the contrary are mostly dependent of chemical and physical properties of the drug and as a consequence are often more difficult to influence and to prevent.

Conclusion

Elderly patients using six or more drugs concomitantly are at risk of potential DRPs. In this study use of NSAIDs and digoxin was associated with the highest risk for potential DRPs. Community pharmacists play

a key role in the identification of potential DRPs in this group of patients. In addition, they have to assume responsibility for the evaluation and prevention of potential DRPs. The classification of potential DRPs into patient-, prescriber- and drug-related can be useful as a tool to focus the effort of intervention. Further study is necessary to establish efficient intervention strategies for elderly at risk for potential DRPs [31, 34].

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