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Classification of drug-related problems

Abstract

Background. Drug-related problems are prevalent and cause considerable patient morbidity and in some cases death, as well as increased health care expenditures. A classification system may contribute to identify such problems, and further to resolve and prevent them.

Material and methods. A draft classification was sent to a broad panel of physicians and pharmacists and comments were requested. Consensus was achieved after two subsequent reviews where structure, content and relevance of the draft were discussed. Mini cases were used for validation of the classification with respect to various professionals' understanding and interpretation of the problem categories.

Results. The classification has a hierarchical structure with six main categories (drug choice, dosing, adverse drug reaction, interaction, drug use and other) and 12 subcategories. The system is relevant for hospitals, general practices, nursing homes and pharmacies. Validation of the system revealed that a majority would assign identical categories to 9/10 cases.

Interpretation. We propose a validated Norwegian classification system for drug-related problems. The system may facilitate improved and more systematic documentation and communication on such problems.

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Drugs are important in prevention and treatment of disease and health complaints. The increasing number of available drugs and drug users, as well as more complex drug regimens lead to more side effects and drug interactions, and complicates follow-up. Drug-related problems (DRPs) lead to substantial morbidity (1) and mortality (2), as well as increased health care expenditure (3), which in turn affect both patients and society. Norwegian and international studies show that nursing homes (4, 5), hospitals (6, 7) and general practices (8, 9) have a high prevalence of such problems, and professionals agree that there is substantial room for improvement. The Ministry for Health and Care Services has requested industry-independent research in this area in a Governmental White Paper (10).

Systematic review of patients' total drug use, in the light of clinical information, is an effective method to identify DRPs and start interventions (4, 5, 11, 12). This is a method currently used in research and clinical practice, especially by clinical pharmacists in hospitals and nursing homes. Definitions and classifications of DRPs differ (13–16), and modified versions of these are often used when documenting clinical interventions. It would be an asset to have a common classification system in research and clinical practice.

We aimed at developing and validating a Norwegian classification system for DRPs based on internationally published systems, clinical experience and a consensus procedure. The classification should be based on unambiguous definitions, be useful in different settings (general practice, hospitals, nursing homes, pharmacies) and contexts (research, clinical practice) and with varying access to relevant clinical information (from patients, medical records, drug charts and prescriptions).

Material and method

Development of a classification system

The process started with a seminar for ten physicians and pharmacists who had experience with medication reviews from research or clinical practice. A working group (authors) developed a draft for classification with a hierarchical structure based on a European system (15), to ensure comparability with international studies.

Elements from a modified Delphi technique were used to further develop the classification. By this method consensus is obtained between independent experts through several rounds of «silent brainstorming» where participants in a «panel» produce ideas individually without discussing them. The ideas are communicated to a group of decision makers who discuss the ideas, adjust the draft and subsequently submit a revised draft to the panel participants. The panel participants and decision makers communicate through e-mail (17). Contrary to classical Delphi technique, the panel participants in this study did not prioritize the various elements according to relevance.

The draft classification was sent to medical and pharmaceutical groups in Norway (October 2005). The receivers were: Norwegian Society for Pharmacoepidemiology, special interest group of clinical pharmacists in the Norwegian Association of Hospital Pharmacists, the e-mail list EYR for general practioners, the five regional Drug Information Centres, the Norwegian Pharmaceutical Association, the Pharmacy Association and the Norwegian Society for Pharmacology

Main message

- A classification system for DRPs has been developed and validated
- The classification is hierarchical and consists of six main categories: drug choice, dosage, adverse drug reaction, interaction, drug use and other
- The system is relevant for different settings: hospitals, general practice, nursing homes and pharmacies

Box 1

Examples of case reports used in the validation of the classification

- A 62-year-old man complains of fatigue. Treatment with mirtazapine was started last week and he now takes 30 mg in the evening. He was already using diazepam 10 mg × 3, as well as zopiclone 5 mg to sleep. Classify this case (case 1: 36 % agreement).
- An 87-year-old woman complains of heavy breathing and swollen legs. She has been diagnosed with atrial fibrillation and post infarction failure. She uses warfarin, ramipril 10 mg and furosemide 40 mg × 2. Previously she has also used a beta-blocker and spironolactone, but these drugs were discontinued because of bradycardia and hypotension. You are not sure about which changes in the patient's medication regimen would be appropriate. Classify this problem (Case 5: 51 % agreement).
- 80-year-old woman living in a nursing home. The patient has arthritis and complains regularly of pain in her back and hips. She uses paracetamol 500 mg × 2. Classify this case (Case 20: 92 % agreement).
- 60-year-old man with diabetes and ischemic heart disease presents a prescription on sildenafil 50 mg to a pharmacy. He also uses isosorbide mononitrate, metformin, glipizide, aspirin, enalapril and metoprolol depot. You point out that sildenafil should not be used with nitrates. Classify this problem (Case 22: 74 % agreement).

and Toxicology. The review group was requested to comment on structure, content, clinical relevance and the wording of the classification, as well as suggest changes. The authors assessed all comments and suggestions from the panel and thereafter adjusted the draft for classification. A revised draft was returned to all respondents (March 2006), but no further comments came up during the second review.

Validation of the classification

Relevant professional groups were invited to participate in validation of the classification. The purpose was to assess whether the panel used the classification system in the same way with respect to allocating various DRPs to relevant categories. The panel consisted of 26 pharmacists and 13 physicians working in hospitals, nursing homes, general practice or pharmacies. Twenty-six short, real case reports were sent to the panel (Box 1). Each report contained at least one specific DRP that the participants were asked to assign the most relevant main or subcategory in the classification. All categories in the classification system were represented in the case reports. If a panel participant had suggested more than one category for one single case report, the result was shown in decimals; for example 0.5 for classification in two categories and 0.3 for three categories. A large Australian study used a similar procedure (16).

Results

Definition and classification of drug-related problems

The expert panel agreed on adapting the definition of DRPs provided by the Pharmaceutical Care Network Europe: «An event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes» (15). In this context, a potential problem means a condition that may cause drug-related morbidity or death if no action is undertaken; an actual problem is manifested with signs and symptoms.

DRPs are divided into six main categories and 12 subcategories (tab 1). The categories are given in an order consistent with drug therapy evaluation in clinical practice.

Validation of the classification system

On average, 70 % (median 70 %, variation 36–99 %) agreement was obtained on the DRP category (tab 2). For 10 of the 26 cases, at least 75 % of the respondents chose the same category and for 24 cases more than half were classified as the same. For 22 cases one or more respondents classified them into different categories. There were no differences between physicians and pharmacists in general, but some of the cases were associated with a more varied classification and for these we found a larger difference both within and between professional groups.

Discussion

A Norwegian system for defining and classifying DRPs is proposed. The system builds on cross disciplinary agreement between physicians and pharmacists from various clinical and scientific positions. The classification is a tool to handle challenges in relation to drug treatment and the system could contribute to improved documentation of various problem areas.

The panel's professional and geographical heterogeneity contributes to the classification system's relevance for various aspects of the drug treatment (prescription, monitoring, use, documentation), for various aims and for different parts of the health services. Although it was a goal to include all Norwegian experts in the field, and it should be simple enough to get an overview of the professional environment in the country, it is possible that not all have been included.

Consensus-based procedures are suitable for integration of research-based and experience-based knowledge. The modified Delphi technique is an established method for development of clinical guidelines and quality indicators (17). This method ensures that various meanings are promoted, independent of the participants' relations, position and status. Communication by e-mail enables participation of experts who are geographically far apart. On the other hand, the method is demanding and lack of discussion may prevent identification of good ideas and elimination of bad ones.

Van Mil and collaborators have assessed 14 published classification systems of DRPs (18). The group points out that classification systems should be validated and also that the results of this procedure should be published. However, only a few of the classifications have been validated. We have gone through a case-based validation procedure among a heterogeneous review panel to assess the content of the classification and to reveal validity (face).

The classification system has an open hierarchical structure that can be adapted and expanded with several categories according to need, setting and access to clinical information. The intention was to construct a general model that comprises many different problem areas and at the same time prioritize simplicity and flexibility rather than in depth detailed descriptions. Previously published classifications have been considered to ensure comparability with international models.

We have chosen to include both actual and potential problems in the definition of DRPs (15). This choice is founded in our understanding of the importance of identifying problems before they have become manifest and thereby prevent a possible negative outcome, as for example lack of effect or increased morbidity. Both potential and actual problems can be identified by conducting regular systematic reviews of patients' total drug use.

The participants in the hearing group agreed that undertreatment («need for additional drug») would be part of the classification system. This problem is not strictly associated with one or more specific drugs, but rather to a presumption of effective treatment or to adherence to guidelines to prevent disease; e.g. anticoagulation after a heart attack. Our view coincides with that of Van Mil and collaborators. They criticize the lack of undertreatment as a category in several published classification systems and point at evaluation of treatment effectiveness of a certain condition as a crucial part of medication reviews (18). However, this presumes access to relevant clinical information such as symptoms and laboratory tests, which in some settings will be inadequate, for example in pharmacies.

Validation of the classification system

Table 1 Classification of drug-related problems

Category	Definition	Example
1. Drug choice 1a Need for additional drug	One or more drugs are missing according to established national/international guidelines. Deviations from guidelines that are based on the patient's individual treatment goals and risk factors are not considered to be DRPs.	Statins after a myocardial infarction. Aspirin after a cerebral stroke. ACE[1] -inhibitor for heart failure. Calcium supplements when using corticosteroids. Untreated/undertreated pain.
1b Unnecessary drug	A drug that is seen as unnecessary if the indication is no longer present, with lack of discontinuation or double prescription of two or more drugs from the same therapeutic group	Antibiotic treatment finalised. Ibuprofen and diclophenac concomitantly. Methenamine in a patient with a permanent catheter.
1c Inappropriate drug choice	Not given reason for deviation from concordance between drug and diagnosis/indication or absolute/relative contraindication because of for example age or comorbidity. Deviations that are based on the patient's individual treatment goal and risk factors are not considered to be DRPs.	NSAID[2] with reduced renal function. Broad-spectred antibiotic for simple infection. Antipsychotic drug for restlessness in dementia. Amitryptiline and other drugs with anticholinergic effect in elderly. ACE[1] -inhibitor with aortic stenosis.
2 Dosing 2a Too high dose 2b Too low dose 2c Sub-optimal dosing scheme	Suboptimal dosing (including dosing time and formulation) according to established national/international guidelines. Deviations that are based on the patient's individual treatment goal and risk factors are not considered to be DRPs.	Too high ACE[1] -inhibitor dose in relation to kidney function. Too low paracetamol dose in relation to symptom-giving arthritis. Nitrates given without nitrate-free period. Diuretics given in the evening.
2d Sub-optimal formulation		Should receive a slow release formulation rather than a direct release tablet, e.g. diuretic or analgesic.
3 Adverse drug reaction (ADR)	Any noxious, unintended, and undesired effect of a drug, which occurs at doses in humans for prophylaxis, diagnosis, or therapy (WHO)	Orthostatic hypotension, instable/falling with use of blood pressure lowering drug. Rhabdomyolysis with use of statin. Rash with use of penicillin.
4. Interaction	An interaction is occurring when the effect of a drug is changed by the presence of another drug, food, drink or some environmental chemical agent. Drug combinations with intended overall effect are not considered to be DRPs.	SSRI[3] and TCA[4] (increased S-concentration of TCA). Furosemide and NSAID[2] (reduced diuretic effect). Furosemide and digitalis (increased effect/toxicity of digitalis with hypokalemia). Drugs and various natural drugs/additives/health products, e.g. St John's wort and warfarin.
5. Drug use 5a Drugs administered by health personnel 5b Drugs administered by the patient	Patients' real drug use deviate from the doctor's prescription with respect to type of drug, dose or scheme. It is a prerequisite that prescriptions are based on a common understanding (concordance) between prescriber and patient (exception: patient with dementia, emergency situation etc.) Problems with logistics are not considered to be DRPs.	The patient had taken a wrong drug or dose or to the wrong time. Crushing of slow release tablet or opening of capsule. Practical problems with opening tablet box, difficulty swallowing, nausea/vomiting. Misunderstanding the instructions for use – need for information/guidance. Problem with generic exchange.
6. Other 6a Need for/lack of monitoring of effect and toxicity of drugs.	Monitoring with respect to effect and toxicity of drugs is not done or does not adhere to guidelines.	Clinical examination, e.g. blood pressure, weight with heart failure. Blood tests, e.g. regular counting of Hbc with clozapine treatment. X-ray
6b Lack of or unclear documentation of the drug chart/prescription		Drug chart / prescription lacks information about drug strength or formulation, as well as instructions for use (dosing scheme etc.). Mistakes in transferring between sources.
6c Other	In general therapy discussions that include several problems and do not belong in any other category.	Discussions on appropriate drug therapy for individual patients, e.g. change dose or add a new drug.

[1] Angiotensin converting enzyme | [2] Non steroid anti-inflammatory agent | [3] Selective serotonin reuptake inhibitors | [4] Tricyclic antidepressants

showed an average of 70 % agreement on choice of category. Limit values had not been predefined as there was not sufficient published material to base such definitions on. Our findings are however in agreement with an Australian validation procedure for classification of DRPs; they found an agreement of 69.9 % (16). For some cases there was a larger variation in the classification. Some were relatively heterogeneous and it was challenging to classify these as one single problem in one single category. It is known that such validations render partition between processes difficult, i.e. problem perception and classification in itself (18). Belonging to a professional group did not affect the choice of category and this is in favour of the categories' lack of ambiguity and the system's robustness.

We considered the agreement to be sufficient to use the classification in research projects and clinical practice, for example in communication between physicians, pharmacists working in clinical settings or pharmacies and with patients. An evaluation and possible revision of the classification should be done after it has been used for a while.

Literature

1. Mannesse CK, Derkx FH, de Ridder MA et al. Contribution of adverse drug reactions to hospital admission of older patients. Age Ageing 2000; 29: 35–9.
2. Ebbesen J, Buajordet I, Erikssen J et al. Drug-related deaths in a department of internal medicine. Arch Intern Med 2001; 161: 2317–23.
3. Ernst FR, Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. J Am Pharm Assoc 2001; 41: 192–9.
4. Furniss L, Burns A, Craig SK et al. Effects of a pharmacist's medication review in nursing homes. Randomised controlled trial. Br J Psychiatry 2000; 176: 563–7.

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Table 2 Validation of the classification system: The panel's (n = 39) assignment of DRP category for 26 cases[1]

	Case number																									
Category	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
1. Drug Choise	13.9	19.5	25.5	25.9	19.7	28.2	31	1.5	31.4	–	1	0.5	–	26.4	33.5	1	34.5	10.5	6	2.5		7.5	0.5	3		3
2. Dosing	4.1	17.5	6.7	10.1	3.1	3.9	6	14	1.3	34	–	5.5	1	0.3	1.8	–	–	1	30	36	0.5	–	–	14	4.8	1.8
3. Adverse Drug Reaction	10.2	–	–	–	–	3.8	1	0.5	0.3	1	–	–	–	7.5	–	–	–	–	–	–	–	1	8	–	13.8	–
4. Interaction	9.4	–	–	–	1.5	0.3	–	19	1	1	–	–	–	4.3	2.5	4.5	1	–	–	–	–	29	–	–	–	–
5. Drug use	0.2	–	3.5	0.8	–	–	–	–	1	1	23.5	33	15.9	–	0.2	–	–	26	1	–	38.5	1.5	23	19	–	27.7
6. Other	1.2	2	3.3	2.2	13.7	2.8	–	4	2	2	13.5	–	22.1	0.5	1	33.5	3.5	1.5	2	0.5	–	–	6.5	2	19.4	4.5
Total number of respondents[2]	39	39	39	39	38	39	38	39	37	39	38	39	39	39	39	39	39	39	39	39	39	39	38	38	38	37

[1] In cases where one participant has assigned more than one category to a case, the result is shown in decimals, for example 0.5 with classification into two categories, and 0.3 for three categories.
[2] The number of responses is lower than 39 when one or more participants have not classified the case.

5. Ruths S, Straand J, Nygaard HA. Multidisciplinary medication review in nursing home residents: what are the most significant drug-related problems? The Bergen District Nursing Home (BEDNURS) study. Qual Saf Health Care 2003; 12: 176–80.
6. Blix HS, Viktil KK, Reikvam A et al. The majority of hospitalised patients have drug-related problems: results from a prospective study in general hospitals. Eur J Clin Pharmacol 2004; 60: 651–8.
7. Mannheimer B, Ulfvarson J, Eklof S et al. Drug-related problems and pharmacotherapeutic advisory intervention at a medicine clinic. Eur J Clin Pharmacol 2006; 62: 1075–81.
8. Granas AG, Bates I. The effect of pharmaceutical review of repeat prescribing in general practice. Int J Pharm Pract 1999; 7: 264–75.
9. Zermansky AG, Petty DR, Raynor DK et al. Randomised controlled trial of clinical medication review by a pharmacist of elderly patients receiving repeat prescriptions in general practice. BMJ 2001; 323: 1340.
10. Governmental White Paper (St.meld.) no. 18. 2004–05 «Rett kurs mot riktigere legemiddelbruk». http://www.regjeringen.no/Rpub/STM/20042005/018/PDFS/ STM200420050018000DDDPDFS.pdf (16.09.2008). (In Norwegian)
11. Viktil KK, Blix HS, Moger TA et al. Interview of patients by pharmacists contributes significantly to the identification of drug-related problems (DRPs). Pharmacoepidemiol Drug Saf 2006; 15: 667–74.
12. Kaboli PJ, Hoth AB, McClimon BJ et al. Clinical pharmacists and inpatient medical care: a systematic review. Arch Intern Med 2006; 166: 955–64.
13. Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. Am J Hosp Pharm 1990; 47: 533–43.
14. Westerlund T, Almarsdottir AB, Melander A. Factors influencing the detection rate of drug-related problems in community pharmacy. Pharm World Sci 1999; 21: 245–50.
15. Pharmaceutical Care Network Europe. PCNE Classification for drug-related problems V5.01. http://www.pcne.org/dokumenter/DRP/PCNE%20classification%20V5.01.pdf (16.09.2008).
16. Pharmacy Guild of Australia. PROMISe Phase One Final report. Hobart: University of Tasmania, 2003. http://beta.guild.org.au/uploadedfiles/Research_and_Development_Grants_Program/Projects/2003–504_fr.pdf (16.09.2008).
17. Jones J, Hunter D. Qualitative research: consensus methods for medical and health services research. BMJ 1995; 311: 376–80.
18. Van Mil JW, Westerlund LOT, Hersberger KE et al. Drug-related problem classification systems. Ann Pharmacother 2004; 38: 859–67.

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