

Hospital prescribing errors: epidemiological assessment of predictors

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Aims To demonstrate an epidemiological method to assess predictors of prescribing errors.

Methods A retrospective case-control study, comparing prescriptions with and without errors.

Results Only prescriber and drug characteristics were associated with errors. Prescriber characteristics were medical specialty (e.g. orthopaedics: OR: 3.4, 95% CI 2.1, 5.4) and prescriber status (e.g. verbal orders transcribed by nursing staff: OR: 2.5, 95% CI 1.8, 3.6). Drug characteristics were dosage form (e.g. inhalation devices: OR: 4.1, 95% CI 2.6, 6.6), therapeutic area (e.g. gastrointestinal tract: OR: 1.7, 95% CI 1.2, 2.4) and continuation of preadmission treatment (Yes: OR: 1.7, 95% CI 1.3, 2.3).

Conclusions Other hospitals could use our epidemiological framework to identify their own error predictors. Our findings suggest a focus on specific prescribers, dosage forms and therapeutic areas. We also found that prescriptions originating from general practitioners involved errors and therefore, these should be checked when patients are hospitalized.

Keywords: hospital prescribing errors, pharmacoepidemiology, predictors

Introduction

Hospitalized patients are exposed to multiple drug treatment often involving potentially harmful drugs [1, 2]. Many prescribed drugs are part of treatment that has originally been initiated by general practitioners. Prescriptions for these drugs are often continued without knowledge about the relevance or potential hazards of polypharmacy [3, 4]. The number of drugs marketed is substantial and superspecialization of clinicians is increasing. Consequently, clinicians' knowledge and clinical experience with prescribed drugs is declining. Potential drug related problems for hospitalized patients are therefore a cause of international concern [2, 5].

Drug related problems are classified into two categories: medication errors (MEs) and adverse drug effects (ADEs)

[2, 8]. MEs occur at five levels: drug selection, prescribing, dispensing, administration, and therapeutic monitoring. ADEs include unintended clinical effects after administration. Drug related problems can result in decreased quality of life, morbidity or mortality. Prevention is thus important. In the Netherlands, clinicians are responsible for preventing MEs in drug selection and for dealing with ADEs. Pharmacists are responsible for dispensing and therapeutic monitoring. Prescribing and administration are joint responsibilities. This situation differs in other countries [6, 7].

The objective of this study was to explore an epidemiological framework to assess predictors of prescribing errors, considering patient, prescriber and drug characteristics.

Methods

Design and data collection

A retrospective explorative case-control study (approximately 1:3) was performed. In two teaching hospitals,

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during 14 consecutive days, all new prescriptions issued for hospitalized patients were collected. Repeat prescriptions were excluded. Based on a power calculation including a randomly chosen potential predictor (desired odds ratio $0.8 < OR > 1.2$, $P < 0.05$), random samples of cases (prescriptions with one or multiple errors) ($n = 449$) and controls (prescriptions without errors) ($n = 1464$) were drawn from a source of 5302 prescriptions (of which 14% with errors and 86% without errors). The total of 1913 prescriptions was used for further analysis.

Outcome measures

Prescribing errors were categorized based on the literature: administrative and procedural errors, dosing errors, and therapeutic errors [9–15]. Therapeutic errors specifically concerning irrational drug treatment regarding a certain indication, involve MEs at the level of drug selection and fall outside the scope of this study.

Errors were independently identified and categorized by two raters based on the hospitals' prescribing policies and the drugs' official patient leaflets: a hospital pharmacist (PvdB) and a clinical pharmacologist (JB).

Exposure measures

Potential predictors of errors included (a) prescriber characteristics (medical specialty; prescriber status: clinician staff, assistant clinician, verbal orders transcribed by nursing staff; prescribing day, prescription lay-out: full medication chart overview or single drug prescription; number of daily prescribed drugs per prescriber; hospital size), (b) patient characteristics (sex; age; number of coprescriptions), and (c) drug characteristics (dosage form; therapeutic area: identified by Anatomical-Chemical-Therapeutic (ATC) code; continuation of preadmission treatment: Yes or No; formulary inclusion: Yes or No; drug age: calculated by the year of introduction to the market; numbers of similar marketed drugs and included in the formulary; formulary restrictiveness: expressed by the percentage of similar marketed drugs that is included in the formulary).

Analysis

We performed a univariable ($P < 0.05$) and multivariable logistic regression analysis based on a conditional stepwise forward logistic regression model ($P < 0.01$), using SPSS[®] 9.0. Crude and adjusted ORs with 95% confidence intervals (95%CI) were calculated. Analysis was performed for overall errors and subsequently, for each subcategory as main outcome measure.

Results

For error identification within subcategories, a kappa of 0.74, 0.90, and 0.83, respectively, was calculated as a measure of agreement between the two raters [16]. As the pharmacist was most closely involved in routine prescribing audit, her classification was eventually used. Table 1 presents detailed information on all prescriptions with one or multiple errors ($n = 449$) that were included in this study and subcategorized into administrative and procedural errors, dosing errors and/or therapeutic errors.

The top three therapeutic areas involved in errors were the central nervous system, the gastrointestinal tract, and the respiratory tract. Prescriptions for drugs acting in these areas accounted for 25% (114/449), 20% (92/449) and 12% (53/449), respectively. The distribution within the top three therapeutic areas involved was similar across the three subcategories of errors. However, with respect to dosing and therapeutic errors, third position was replaced by cardiovascular and infectious diseases, respectively.

Table 2 presents the findings of the multivariable analysis. Across all error subcategories, only prescriber and drug characteristics were associated with errors. After univariable analysis, the number of drugs prescribed daily per prescriber and the weekday of prescribing appeared predictors of errors. However, after multivariable analysis, associations disappeared. Patient characteristics were not associated with errors. Whether the prescribed drug was included in the hospital formulary, the numbers of similar drugs included in the formulary and marketed, the degree of formulary restrictiveness per drug group and the time elapsed since the drug was introduced, were not predictors of errors.

Conclusions

Our findings suggest that protection of hospitalized patients against prescribing errors requires a focus on prescriptions taking account of certain prescribers, dosage forms, and therapeutic areas. Many errors involve continued prescriptions initiated in general practice. The need for improved communication regarding prescribed drugs is obvious. Our findings refer to the participating hospitals only. Nevertheless, they are in line with other studies [9, 11, 14, 18–20, 23]. However, differences between hospitals, regions and countries are inevitable and the epidemiological framework presented here could be used to explore predictors in other hospitals.

A strength of this explorative study is the directness of the epidemiological method including different kinds of predictors and comparing erroneous with non-erroneous prescriptions. This approach has not previously been validated in European settings. Prescribers' unawareness of the study is expected to have reduced potential

Table 1 Hospital prescriptions with errors ($n=449$).

Subcategory	n	(%) of all prescriptions with errors (n = 449)†	Examples
<i>Administrative and procedural errors</i>	245	(55)	
General level			
Unreadable prescription	14	(3)	Obvious
Prescription date or start date unclear	25	(6)	Obvious
Non-drug information on the prescription	2	(<1)	'Patient was asleep at 1.00 a.m.'
Patient level			
Patient data incomplete/unclear	4	(1)	Patient identification impossible
Patient mix-up	1	(<1)	Obvious
Non-existing patient	5	(1)	Patient already discharged or deceased
Prescriber level			
Prescriber data missing/unclear	7	(2)	Department identification impossible
Department mix-up	11	(2)	Patient moved to other department
Prescriber signature missing/unclear‡	64	(14)	Obvious
Drug level			
Drug name missing/unclear	20	(5)	'Atoratin': instead of Atorvastatin
Drug name mix-up	5	(1)	'Phenytoin' instead of Phenylephrine
Unauthorized abbreviation	8	(2)	'TCA': trichloric acid or triamcinolon acetonide?
Amount of drug missing/unclear	13	(3)	'Tretinoin cremor': 20 g or 5 g?
Administration level			
Dosage form missing/unclear or mix-up	33	(7)	'Salbutamol inhaler': rotacaps, rotadisk or aerosol?
Non-existing dosage form	15	(3)	'Diclofenac inhaler'
Route missing/unclear or mix-up	26	(6)	'Pilocarpin 2 dd 2 dr': which eye(s)?
<i>Dosing errors</i>	282	(63)	
Non-existing strength	18	(4)	'Ondansetron 50 mg'
Strength missing/unclear	41	(9)	'Levothyroxin 2 dd 1 tablet': 0.25 or 0.125?
Dosing frequency incomplete/unclear	27	(6)	'1 dd 20 mg + 20 mg, but not 40 mg'
Wrong dosing frequency (time schedule)	11	(2)	'Temazepam 20 mg 2 dd 1 (8 + 10 a.m.)'
Overdosing (supratherapeutic)	67	(15)	
Maximum daily dose missing/unclear	48	(11)	'2 ml Pethidin 50 mg ml ⁻¹ , as needed'
Maximum daily dose exceeded	19	(4)	'Digoxin 0.25 mg' 3 dd 3 tablets
Underdosing (subtherapeutic)	29	(6)	'Flucloxacillin 50 mg' 1 dd 1 capsule
Duration of therapy unclear/exceeded	22	(5)	'Xylometazolin 0.5 mg 3 dd 2 dr for 3 weeks'
<i>Therapeutic errors</i>	58	(13)	
Contra-indication (including allergy)	8	(2)	Cisapride for arrhythmic patient
Drug-Drug interaction	24	(5)	Magnesiumoxide and ferrofumarate coprescribed
Ineffective monotherapy	4	(1)	Flucytosine monotherapy
(Pseudo) Duplicate therapy	22	(5)	Temazepam and oxazepam

†: One prescription may involve multiple errors; ‡: Dutch legal implication that dispensing is prohibited.

underestimation of errors. Potential classification bias is a weakness of our study, although this was minimized by using patient information sheets as a reference to identify errors. Furthermore, we were unable to include the clinical experience of prescribers. However, we used their status to partly account for this.

The reported incidence of prescribing errors varies from 3 to 169 per 1000 prescriptions. These figures depend strongly on study design and particularly, on the definition of 'error' and the clinical relevance [2, 8, 9, 11, 14, 17, 31]. Our findings agree with other studies showing that missing and incorrect doses are the most common errors whereas patient mistakes are rare [11, 14, 18–20]. Our data link

with others showing that analgesic, cardiovascular, and gastrointestinal drug groups are most frequently involved [11, 13, 15]. However, they do not support observations indicating that infectiology is a troublesome area [11, 14, 15, 18]. Instead, we identified oncological and topical therapy (dermatological and ophthalmologic), and inhalation devices prescribed by nonpulmonologists as predictors. These involve individual-based dosing or a wide variety of specific dosage forms, implying nonstandardized dosing and the risk of confusion. To our knowledge these potential predictors have not previously been validated.

As for the medical specialties involved, paediatrics, geriatrics, and intensive care medicine are supposed to be

Table 2 Predictors of prescribing errors: Multivariable case-control analysis ($n=1913$)†.

Predictor	Overall errors		Administrative and procedural errors		Dosing errors		Therapeutic errors	
	OR _{adj}	95% CI	OR _{adj}	95% CI	OR _{adj}	95% CI	OR _{adj}	95% CI
<i>Prescriber characteristics</i>								
<i>Medical specialty‡</i>								
Cardiology	NS	–	NS	–	NS	–	NS	–
Geriatrics	NS	–	NS	–	NS	–	NS	–
Gynaecology and obstetrics	1.81	1.11, 3.00	NS	–	3.76	2.27, 6.23	NS	–
Internal medicine	NS	–	2.10	1.42, 3.12	1.84	1.30, 2.59	NS	–
Intensive care medicine	NS	–	NS	–	0.17	0.05, 0.63	NS	–
Neurology	NS	–	NS	–	NS	–	NS	–
Oncology	NS	–	NS	–	NS	–	NS	–
Orthopaedics	3.36	2.08, 5.41	5.30	3.12, 9.04	1.90	1.13, 3.22	NS	–
Paediatrics and neonatology	NS	–	NS	–	NS	–	NS	–
Psychiatry	NS	–	NS	–	NS	–	NS	–
Pulmonology	0.53	0.36, 0.78	NS	–	NS	–	NS	–
Surgery	NS	–	NS	–	1.91	1.24, 2.97	NS	–
Urology	NS	–	NS	–	NS	–	NS	–
<i>Prescriber status</i>								
Clinician staff (Ref)								
Assistant clinician	1.57	1.15, 2.14	NS	–	NS	–	NS	–
Nursing staff ††	2.53	1.77, 3.62	NS	–	3.23	2.19, 4.77	2.60	1.24, 5.45
Total number of prescribed drugs	NS	–	NS	–	NS	–	NS	–
Prescribing day	NS	–	NS	–	NS	–	NS	–
<i>Hospital size</i>								
Large >500 beds (Ref)								
Small ≤500 beds	0.73	0.56, 0.95	0.34	0.22, 0.51	NS	–	NS	–
<i>Prescription lay-out:</i>								
Full medication overview (Ref)								
Single drug prescription	NS	–	NS	–	NS	–	1.58	1.29, 1.84
<i>Patient characteristics</i>								
Sex	NS	–	NS	–	NS	–	NS	–
Age	NS	–	NS	–	NS	–	NS	–
Total number of coprescriptions	NS	–	NS	–	NS	–	NS	–
<i>Drug characteristics</i>								
<i>Dosage form</i>								
Eye preparations	11.1	4.34, 28.5	4.21	1.44, 12.3	7.57	2.37, 24.1	NS	–
Inhalation devices	4.10	2.55, 6.62	3.15	1.10, 9.00	2.52	1.43, 4.47	NS	–
Topical applicatives	2.41	1.20, 4.85	NS	–	NS	–	NS	–
Oral preparations	NS	–	NS	–	NS	–	NS	–
Parenteral solutions	NS	–	NS	–	NS	–	0.31	0.11, 0.88
Rectal preparations	1.76	1.04, 2.97	NS	–	NS	–	NS	–
<i>Therapeutic area (ATC code)</i>								
Gastrointestinal tract (A)	1.69	1.20, 2.38	NS	–	2.29	1.57, 3.34	NS	–
Blood system (B)	NS	–	NS	–	NS	–	NS	–
Cardiovascular tract (C)	NS	–	NS	–	NS	–	NS	–
Hormonal systemic therapy (H)	NS	–	NS	–	NS	–	NS	–
Infections (J and P)	NS	–	NS	–	NS	–	NS	–
Cancer therapy (L)	2.59	1.03, 6.53	NS	–	3.29	1.13, 5.34	NS	–
Musculo-skeletal system (M)	NS	–	NS	–	NS	–	3.34	1.07, 10.5
Nervous system (N)	1.73	1.26, 2.37	NS	–	1.76	1.20, 2.58	2.33	1.24, 4.40
Respiratory tract (R)	NS	–	3.11	1.20, 8.11	NS	–	NS	–
Other: topical therapy (D, G, S)	NS	–	NS	–	2.64	1.30, 5.34	NS	–
<i>Continued pre-admission drug</i>								
No, hospital initiated (Ref)								
Yes, general practice initiated	1.74	1.33, 2.29	NS	–	1.68	1.23, 2.31	NS	–

Table 2 (Cont.)

Predictor	Overall errors		Administrative and procedural errors		Dosing errors		Therapeutic errors	
	OR _{adj}	95% CI	OR _{adj}	95% CI	OR _{adj}	95% CI	OR _{adj}	95% CI
Drug included in HDF (Yes or No)	NS	–	NS	–	NS	–	NS	–
Drug Age/Year of marketing	NS	–	NS	–	NS	–	NS	–
Number of fellow drugs on the market	NS	–	NS	–	NS	–	NS	–
Number of fellow drugs in the HDF	NS	–	NS	–	NS	–	NS	–
HDF Restrictiveness	NS	–	NS	–	NS	–	NS	–

†: The level of statistical significance was set at $P=0.05$ (χ^2 testing); The multivariable model for each category of errors was constructed by performing stepwise forward logistic regression analysis. Adjustment was done for all possible confounding factors that significantly contributed to the model. Non-significant factors (NS) were not adjusted for. ‡: All other medical specialties as reference. ††: Verbal orders transcribed by nursing staff.

the most frequently involved in errors. However, our findings show that these medical specialties are significantly less associated with errors [11, 14, 15, 18, 19, 21]. Instead, we identified surgery, gynaecology and obstetrics, and orthopaedics. These specialties rarely initiate drug treatment outside their own therapeutic area, and generally, knowledge about and interest in drugs may be poor [15, 28]. However, within paediatrics, geriatrics and intense care medicine, drug treatment is important. Moreover, patients from these specialties are at high risk of drug related problems due to complex pathology, morbidity and pharmacokinetics [18, 19, 21, 22]. Apparently, these considerations are taken into account in our participating hospitals. The reason for internists to be associated with particular dosing errors may relate to their involvement with a wide range of therapeutic areas.

Our data confirm that nursing staff [23, 24], as well as assistant clinicians [11] are associated with errors. Findings that weekday and prescription volume are associated with errors could not be confirmed [11, 23]. Our findings support suggestions to use full medication chart overviews for prescribing. In this way potential drug–drug interactions cannot slip away from the attention of prescribers which is the case when using single drug prescriptions [13]. Dutch hospital formularies provide detailed prescribing information on all (new) drugs included, thereby intending to reduce errors. Our findings suggest that this intention is of a theoretical nature only.

The impact of hospital prescribing on prescribing in general practice is substantial and has been documented [25, 31]. Without adequate information transfer between healthcare professionals at hospital discharge, patients are at risk of exposure to MEs in the case of repeat prescriptions [4, 12]. Conversely, the impact of general practitioners prescribing on hospital prescribing has also been demonstrated [3, 26]. Our findings show that the risk of errors also exists in this opposite direction of crossing the interface between primary and secondary healthcare, on

hospital admission. On admission, confusion about current preadmission treatment exists and dosing of preadmission drugs is often continued based on patient memory without further verification at his or her community pharmacy. In due time, in the Netherlands, hospitals will introduce computerized prescribing and electronic pharmacotherapeutic information transfer between sectors [7, 27, 29, 30].

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