Compliance with National Guidelines for the Management of Drug–Drug Interactions in Dutch Community Pharmacies

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BACKGROUND: Pharmacists contribute to the detection and prevention of drug therapy–related problems, including drug–drug interactions. Little is known about compliance with pharmacy practice guidelines for the management of drug–drug interaction alerts.

OBJECTIVE: To measure the compliance of community pharmacists with Dutch guidelines for the management of drug–drug interactions and to determine patient- and prescriber-related determinants for noncompliance.

METHODS: Sixteen clinically relevant drug–drug interactions were included in the study based on certain described criteria. From June to August 2005, Dutch pharmacists (N = 149) collected alerts occurring in daily patient care for these interactions as well as information related to the patient, the alert itself, the prescriber, and the management of the alert. Noncompliance was measured by comparing the management executed by the pharmacy with the national guidelines.

RESULTS: Overall compliance with the guidelines was 69.3% (n = 423), with large differences between the various drug–drug interactions. Male sex (OR 2.25; 95% CI 1.52 to 3.31), oldest age (>75 y; OR 1.97; 95% CI 1.03 to 3.75), and polypharmacy (>7 medications; OR 2.35; 95% CI 1.46 to 3.80) were associated with a higher probability for noncompliance with the guidelines. Prescriber-related variables had no significant influence on guideline compliance. Substitution of one of the involved agents, recommended for most of the drug–drug interactions, was executed in a small minority of cases. The outcome of interaction management, such as substitution, dose reduction, or temporary stop of one of the agents, was frequently inconsistent with the guidelines. Compliance rates were partly influenced by the ultimate decision made by the prescriber. In that way, pharmacies' compliance was not solely assessed. However, in only 22.5% of the cases was the drug–drug interaction presented to the prescriber.

CONCLUSIONS: Noncompliance with Dutch guidelines for the management of drug–drug interaction alerts is common in community pharmacies. Further research into underlying reasons for noncompliance is warranted, such as the relation between pharmacist and prescriber in this context.

KEY WORDS: compliance, drug–drug interaction, drug related problem, guideline, intervention, pharmaceutical care, pharmacist, risk management.

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A consistent finding in research of health services is the gap between available evidence and clinical practice. It is estimated that 30–40% of patients do not receive care according to current scientific evidence.[1] Contrary to medical practice, very little is known about compliance with pharmacy practice guidelines, particularly those concerning the management of drug–drug interaction alerts.

Pharmacists contribute to the detection and prevention of drug therapy–related problems including medication errors, the occurrence of which has been the subject of several studies and part of a public debate about patient safety.[2-5] The negative impact of one type of drug therapy–related problems, drug–drug interactions, on drug related morbidity has been repeatedly demonstrated.[6-8]

In the Netherlands, 2 guidelines for the management of drug–drug interactions have been developed and are kept up to date by 2 working groups on the basis of published evidence of drug–drug interactions.[9] This evidence is transformed into alerts with concrete recommendations for their management that are incorporated into community pharmacy software programs for prescription processing. The software program checks new prescriptions for drug–drug interactions using

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stored information about drugs that will be dispensed simultaneously or have already been dispensed to the patient. The objective of our study was to determine the compliance rate of community pharmacists to national guidelines for the management of drug–drug interaction alerts as well as patient- and prescriber-related determinants for noncompliance.

Methods

SETTING AND STUDY POPULATION

All Dutch community pharmacies using the Pharmacom information technology system (N = 791) were invited (once, via mail) to participate in this study, of which 172 (21.7%) responded positively. Ultimately, several pharmacies decided not to participate due to heavy workload, and 149 (18.8%)—serving approximately 1.4 million patients, which is almost 9% of the Dutch population—were included in this study. During a 3 month period (June–August 2005) each participating pharmacy was requested to collect alerts of drug–drug interactions selected for this study (see below) as encountered during routine daily patient care. The participating pharmacies received a pretested study protocol and the coordinating research center was available for questions throughout the study. The work was conducted in compliance with the requirements of the institutional review board of the Department of Pharmacoepidemiology and Pharmacotherapy, Utrecht University.

SELECTION OF THE DRUG–DRUG INTERACTIONS INCLUDED

The Pharmacom information technology system monitors approximately 300 different types of drug–drug interactions.[10] For our study we selected interactions that fulfilled the following criteria: the available evidence had to be classified as 3 or higher, and the clinical relevance had to be classified as C or higher, according to the classification system developed and maintained by a working group of the Scientific Institute of Dutch Pharmacists (WINAp) that has been described in detail elsewhere.[9] In brief, within that classification system, drug–drug interactions are classified on a 6 point relevance scale ranging from not serious to very life-threatening (category A–F, respectively) and on a 5 point evidence scale ranging from not proven to very well proven (category 0–4, respectively). In other words, all the included drug–drug interactions had to have potentially harmful consequences. An additional criterion was that the management of these drug–drug interaction alerts according to the national guidelines had to involve the substitution of one of the interacting drugs, which was sometimes presented as the only option and sometimes accompanied by an alternative option. This led to the inclusion of 16 drug–drug interactions (Table 1). An important feature of the selected drug–drug interactions is the relatively low frequency of recurrent alerts, because of the nature of one of the interacting agents (eg, antibiotics, antimycotics, phosphodiesterase type 5 [PDE-5] inhibitors). This decreased the chance that the drug–drug interaction had already been managed in the past for the same patient.

COLLECTION AND CLASSIFICATION OF DATA

A computer program was developed enabling each pharmacy to extract and collect the selected drug–drug interaction alerts that had occurred during the previous week. These data extractions were subsequently sent by the pharmacist to the coordinating research center electronically. On the first day of the week the pharmacist was requested to execute the data extraction and to send the data to the research center. On the third, fourth, and fifth day this procedure was repeated. For each drug–drug interaction alert sent to the research center, a questionnaire was returned to the community pharmacy by email. Subsequently, completed questionnaires were sent to the research center by email, postal mail, or fax.

On the questionnaire form, pharmacists, who had not all been necessarily involved with the drug–drug interaction alert, recorded information related to the patient (age, sex, estimated current drug use), the alert itself (medicines involved, same or different prescribers for the interacting drugs, type of prescriber of latest prescription [ie, general practitioner or specialist]), and information about the management of that drug–drug interaction alert by the pharmacy. Management was categorized as external action or no external action. External action was defined as an intervention directed at the prescriber, advice given to the patient, or other, such as communication with the anticoagulation clinic. The specific external action or its outcome had to be specified. Some examples of specific action taken or their outcome include the substitution of one of the interacting medicines, a dose change of one of the interacting medicines, or advice to obtain plasma concentrations (eg, potassium) related to drugs.

In case internal pharmacy procedures did not require external action, the respondent was asked to give reasons for that (eg, recurrent alert or alert already managed in the past).

COMPLIANCE WITH GUIDELINES

Table 1 summarizes the management guidelines for the selected drug–drug interactions presented to pharmacists on the computer screen each time that the drug–drug interaction alert occurs, as well as in a yearly updated textbook.[10] A working group of Health Base Foundation, a knowledge center closely connected to the Pharmacom information technology system, is responsible for the content of this textbook, which provides background information about several drug therapy-related problems, such as drug–drug

interactions and drug–disease interactions. Moreover, algorithmic strategies for management are provided, which were used as the gold standard for the evaluation of the management of drug–drug interactions by pharmacists. The comparison between the management output as described on the questionnaires and the guideline was made by one of the authors (HB) and checked by another (TS). The outcome of this comparison was threefold: compliant, noncompliant, or uncertainty as to assessment. Finally, the association between noncompliance with the guidelines and several patient-related characteristics (ie, sex, age, number of drugs in use) and prescriber-related characteristics (different prescribers for the interacting drugs, prescriptions prescribed during different consultations, latest prescription from other prescriber [ie, not general practitioner]) was examined.

DATA ANALYSIS

Data were analyzed using standard descriptive data analysis (SPSS version 12.0, SPSS Inc., Chicago, IL). Logistic regression analysis was used to estimate the strength of the association between characteristics and noncompliance with the guideline.

Table 1. Description of Guidelines for the Management of 16 Drug–Drug Interactions

Interaction	Possible Consequences	Proposed Management
Statins–macrolides	myopathy, rhabdomyolysis	macrolide only for 1 day: pt. instructed to contact physician immediately in case of severe myopathy; in other cases: stop or reduce dose of simvastatin or atorvastatin during macrolide course (maximum 20 mg and 40 mg, respectively); no known problems with fluvastatin, pravastatin, or rosuvastatin; when maintaining use of low-dose statin: pt. instruction given as above
Statins–antimycotics	myopathy, rhabdomyolysis	at start of statin: postpone use of statin until end of antimycotic course or choose pravastatin or rosuvastatin; at start of fluconazole ≤200 mg/day: no action; at start of fluconazole >200 mg/day or other antimycotic: substitute another antimycotic (eg, terbinafine), temporarily stop statin, or change to pravastatin or rosuvastatin
Coumarins–TMP/SMX	bleeding	substitution for TMP/SMX or warning to anticoagulation clinic via fax[a]
Digoxin–macrolides	digoxin toxicity	substitution for macrolide (with high serum digoxin level as risk factor, daily dose ≥0.25 mg)
PDE-5 inhibitors–nitrates	drop in systolic and diastolic blood pressure	substitution for PDE-5 inhibitor; in case of maintenance treatment with nitrate: substitution with β-blocker
Theophylline–macrolides	theophylline toxicity	at start of macrolide: substitution for macrolide or monitor theophylline serum level[b]; at start of theophylline: begin with low dose, later dose increase guided by serum concentration
Coumarins–antimycotics	bleeding	fluconazole (1 day course): no intervention; other regimens of azole antimycotics: substitution (particularly miconazole, fluconazole, or voriconazole) or warning to anticoagulation clinic via fax[a]
TCAs–terbinafine	TCA toxicity	at start of TCA: low dose of TCA to maximum of 50 mg daily; older pts.: 25 mg daily; at start of terbinafine: substitution for terbinafine or dose reduction of TCA to maximum of 50 mg daily; older pts.: 25 mg daily (starting dose regimens and dose reductions of TCA preferably guided by serum concentration control)
Theophylline–quinolones	theophylline toxicity	substitution for quinolone (not by macrolide) or dose decrease of theophylline to 50% in case of ciprofloxacin or pipemidic acid
Phenytoin–TMP/SMX or trimethoprim or sulfonamides	phenytoin toxicity	at start of TMP/SMX or trimethoprim or sulfonamides: substitution by another antibiotic (no fluoroquinolone); at start of phenytoin: begin with low dose, later dose increase guided by serum concentration/clinical effect
Methotrexate– TMP/SMX or trimethoprim	bone marrow suppression	substitution for TMP/SMX or trimethoprim (no safe time interval is known)
Digoxin–itraconazole	digoxin toxicity	substitution for itraconazole or dose decrease of digoxin, guided by serum concentration
PDE-5 inhibitors–CYP3A4 inhibitors	sildenafil or vardenafil toxicity	sildenafil–ritonavir: avoidance of sildenafil or dose reduction to maximum of 25 mg over 48 h; sildenafil–other CYP3A4 inhibitors: dose reduction of sildenafil to maximum of 25 mg over 48 h; vardenafil–indinavir or very strong CYP3A4 inhibitors: avoidance of vardenafil or substitution of CYP3A4 inhibitor; vardenafil–other CYP3A4 inhibitors: dose reduction of vardenafil to maximum of 5 mg over 24 h
Carbamazepine–macrolides	carbamazepine toxicity	substitution for CYP3A4 inhibiting macrolide (ie, erythromycin, clarithromycin)
Terfenadine–QT interval prolonging drugs	QT interval prolongation ventricular arrhythmias	substitution for terfenadine by other antihistaminic agent
St. John's wort–digoxin	digoxin toxicity	avoidance of combination

PDE-5 = phosphodiesterase type 5; TCA = tricyclic antidepressant; TMP/SMX = trimethoprim/sulfamethoxazole.
[a]A warning to the patient or the patient's relative was also assessed as compliance; every patient had access to the clinic's telephone number.
[b]A warning to the patient was also assessed as compliance.

Results

Of the 858 returned questionnaires, all cases concerning unjustified alerts (n = 97; mostly because the first drug had already been stopped) and all alerts missing essential information (n = 17) were excluded from the analysis. The remaining 744 drug– drug interaction alerts were collected by 149 pharmacies, with a range of 1–17 alerts per pharmacy (average 5). The alerts involved an approximately equal number of males (n = 309) and females (n = 301). The mean ± SD age was 64.5 ± 14.7 years (range 2–99). The number of drugs used at the time of the alert was 6.4 ± 3.3 (range 0–22), excluding dermatologic preparations. The frequency of alerts for the 16 included drug– drug interactions (Table 2) was variable, ranging from 205 alerts for statin–macrolide interaction to 1 alert for a St John's wort– digoxin interaction. One-hundred thirty-four cases (18.0%) could not be evaluated because they contained, primarily, a recurrent alert with no information about its management.

Of all alerts for which an assessment was possible (n = 610), pharmacists undertook external action in 79.5% (n = 485; Figure 1). In case of external action, the prescriber was consulted in 28.2% (n = 137), advice was given to the patient in 72.8%, and another action was undertaken in 14.4%, mainly information giving to the anticoagulation clinic. Twofold actions occurred several times.

Overall compliance with the guideline was 69.3% (n = 423) with highly variable rates depending on the type of interaction. A high compliance rate was found for interactions involving coumarin anticoagulants (92.5% and 95.8%). Compliance was also relatively high for tricyclic antidepressants–terbinafine (90.9%), statins–macrolides (89.8%), statins–antimycotics (82.2%), and PDE-5 inhibitors–CYP3A4 inhibitors (75.0%). A relatively low compliance rate was found for interactions involving theophylline (45.0% and 21.6%), digoxin–macrolides (8.9%), and PDE-5 inhibitors–nitrates (2.8%).

The degree of compliance also varied with management recommendations. For alerts for which substitution was the only proposed management option, we found low compliance (9.2%) with the guideline (digoxin–macrolides, methotrexate/trimethoprim/sulfamethoxazole or trimethoprim, carbamazepine–macrolides, terfenadine–QT interval prolonging agents, St. John's wort– digoxin). For alerts for which a clear alternative option was possible in addition to substitution, the compliance amounted to 82.2% (statins–macrolides, statins–antimycotics, coumarins–trimethoprim/sulfamethoxazole, theophylline–macrolides, coumarins–antimycotics, tricyclic antidepressants– terbinafine, theophylline–quinolones, digoxin–itraconazole).

A temporary stop of one of the agents was executed in 30 cases (4.9%), 19 (63.3%) of which were consistent with the guidelines. Dose adjustment was performed in 17 cases (2.8%), of which about half (8 cases) were in accordance with the guidelines.

The association between patient- and prescriber-related variables and noncompliance with the guidelines is presented in Table 3. Adjusted for all other variables, male sex (OR 2.25; 95% CI 1.52 to 3.31), the highest age category (>75 y; OR 1.97; 95% CI 1.03 to 3.75), and current use of more than 7 medications (OR 2.35; 95% CI 1.46 to 3.80) indicate a higher probability for noncompliance concerning the whole group of selected drug– drug interactions. Prescriber-related variables, such as different prescribers for both drugs,

Table 2. Compliance with the Guidelines for Management of 16 Drug–Drug Interactions

Interaction	Pts., n	Uncertainty as to Assessment, n (%)	Compliance after Adjustment,[a] %
Statins–macrolides	205	8 (3.9)	89.8 (177/197)
Statins–antimycotics	119	12 (10.1)	82.2 (88/107)
Coumarins–TMP/SMX	90	18 (20.0)	95.8 (69/72)
Digoxin–macrolides	75	19 (25.3)	8.9 (5/56)
PDE-5 inhibitors–nitrates	62	26 (41.9)	2.8 (1/36)
Theophylline–macrolides	53	16 (30.1)	21.6 (8/37)
Coumarins–antimycotics	49	9 (18.3)	92.5 (37/40)
Tricyclic antidepressants–terbinafine	34	12 (35.3)	90.9 (20/22)
Theophylline–quinolones	24	4 (16.7)	45.0 (9/20)
Phenytoin–TMP/SMX or trimethoprim or sulfonamides	10	4 (40.0)	50.0 (3/6)
Methotrexate–TMP/SMX or trimethoprim	7	4 (57.1)	33.3 (1/3)
Digoxin–itraconazole	5	1 (20.0)	50.0 (2/4)
PDE-5 inhibitors–CYP3A4 inhibitors	5	1 (20.0)	75.0 (3/4)
Carbamazepine–macrolides	3	0 (0.0)	0 (0/3)
Terfenadine–QT interval prolonging drugs	2	0 (0.0)	0 (0/2)
St. John's wort–digoxin	1	0 (0.0)	0 (0/1)
TOTAL	744	134 (18.0)	69.3 (423/610)

PDE-5 = phosphodiesterase type 5; TMP/SMX = trimethoprim/sulfamethoxazole.
[a]Minus cases with uncertainty as to assessment.

were not shown to have significant influence on the noncompliant management of drug–drug interaction alerts.

Discussion

To our knowledge, this is the first multicenter study evaluating compliance with national guidelines concerning the management of drug–drug interaction alerts in community pharmacies. The overall compliance rate amounted to 69.3%. The degree of compliance varied with the nature of the drug–drug interaction, patient characteristics, and the nature of the recommended management actions in the guidelines.

The degree of and variation in noncompliance with clinical guidelines in our study matches the outcomes of studies concerning medical practitioners' compliance with di-

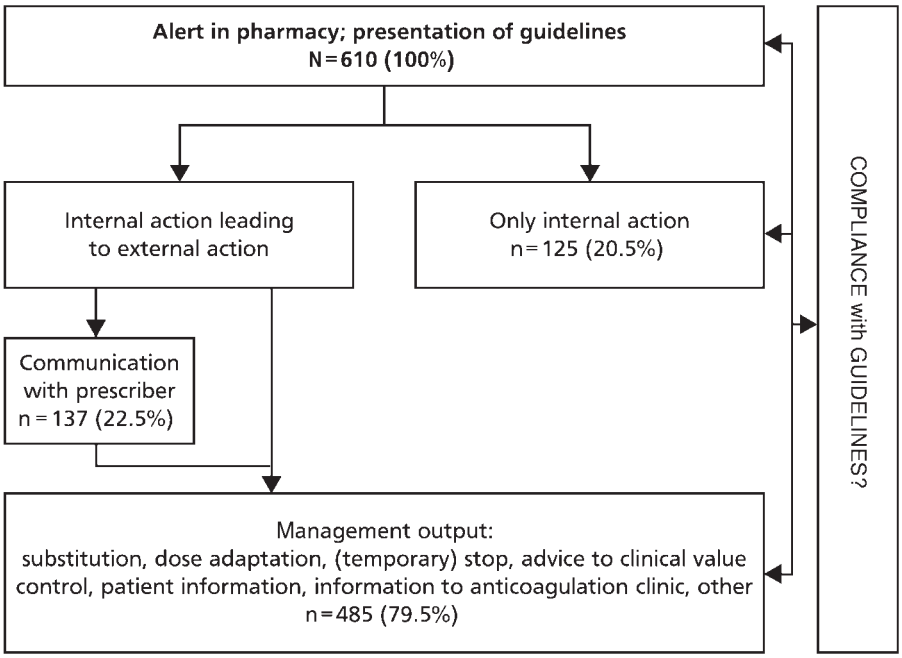

Figure 1. Alert management in Dutch community pharmacies of 16 potentially harmful drug–drug interactions.

Table 3. Determinants for Noncompliance of Pharmacists with Guidelines for Management of Drug–Drug Interactions

Characteristic	Compliance with Guidelines, n (%)[a]		OR (95% CI)	
	Noncompliant n = 187	Compliant n = 423	Crude	Adjusted[b]
Patient-related				
Sex, male	117 (62.6)	192 (45.4)	2.05 (1.44 to 2.93)	2.25 (1.52 to 3.31)
Age, y				
0–50	22 (11.8)	73 (17.3)	(reference)	1 (reference)
51–65	55 (29.4)	136 (32.2)	1.34 (0.76 to 2.37)	1.25 (0.67 to 2.34)
66–75	53 (28.3)	127 (30.0)	1.39 (0.78 to 2.46)	1.24 (0.66 to 2.33)
>75	56 (29.9)	85 (20.1)	2.19 (1.22 to 3.92)	1.97 (1.03 to 3.75)
Drugs in use, n				
0–4	43 (23.0)	151 (35.7)	(reference)	1 (reference)
5–7	59 (31.6)	137 (32.4)	1.51 (0.96 to 2.39)	1.51 (0.93 to 2.45)
>7	80 (42.8)	124 (29.3)	2.27 (1.46 to 3.52)	2.35 (1.46 to 3.80)
Prescriber-related				
Different prescribers for interacting drugs	59 (31.6)	136 (32.2)	1.01 (0.69 to 1.46)	1.00 (0.62 to 1.61)
Prescriptions during different consultations	166 (88.8)	383 (90.5)	0.81 (0.46 to 1.41)	0.78 (0.42 to 1.45)
Latest prescription from other prescriber (mostly specialist), not general practitioner	43 (23.0)	106 (25.1)	0.90 (0.60 to 1.35)	0.77 (0.46 to 1.30)

[a]Not all values total 100% because of missing values.
[b]Adjusted for all other characteristics.

agnostic or therapeutic guidelines.[1,11,12] However, it is questionable whether this issue concerning pharmacists' compliance can be fully compared with the outcomes of other professionals. An important difference in our study on drug–drug interactions is that pharmacists must sometimes present the problem with some management options to the prescriber, who ultimately decides on the management of the drug–drug interaction. In our study, pharmacists directly discussed the problem with the prescriber in 22.5% of the cases (n = 137); the compliance rate of these cases was lower (56.2%; n = 77) than the average compliance rate in the study (69.3%; n = 423).

There were considerable differences in the quality of the compliant as well as the noncompliant management of pharmacists, which we describe to some extent and illustrate by using examples from this study. Compliant management can imply a rigorous intervention, meaning, for instance, contact with the prescriber as well as communication with the patient and with a substitution of one of the interacting drugs as an outcome. However, compliant management can also imply no action, for example, in case of a 1 day course of fluconazole (interaction: coumarins–antimycotics). The same applies to noncompliant interventions. We found superfluous interventions, such as a warning to the anticoagulation clinic in case of a 1 day course of fluconazole combined with a coumarin anticoagulant. However, we also found interventions that could be considered potentially doubtful or even potentially negative concerning patient outcomes. Examples were a temporary stop of digoxin use and a temporary stop of theophylline use. Finally, it must be emphasized that some noncompliant outcomes of interventions made by pharmacists, which were mostly in concordance with the prescriber, were certainly realistic: low dosage of digoxin with relatively young age, rise of serum concentration assessed as not problematic because the physician was just about to increase the dosage (carbamazepine), substitution of terbinafine tablet by terbinafine creme.

There are several possible reasons for guideline noncompliance. We cannot exclude that the relation with the prescriber might have affected the intervention. Substitution of one of the interacting drugs was executed in a limited number of cases, even when substitution was the only proposed intervention. Perhaps many pharmacists find substitution of one of the interacting drugs a difficult and time-consuming type of management, because it requires intervention toward the prescribing physician. In other studies, interprofessional barriers have been identified concerning the relationship between community pharmacists and physicians.[13] In a majority of cases, more easily applicable management options were preferred, such as a warning to the anticoagulation clinic, temporary stop of a statin, or dose reduction of one of the medicines, mostly without interference of the prescriber. Nevertheless, a Dutch study revealed that pharmacists and general practitioners largely agree on the surveillance role that a pharmacist should fulfill.[14] In addition, we observed that in several instances the prescriber ultimately decided not to change one of the prescribed medicines as recommended. It is an intriguing question whether this is associated with the decision frequently made by physicians to override drug–drug interaction alerts[15] and/or with a lack of professional persuasiveness of the pharmacist. Continued scientific inquiry is needed regarding pharmacists' and physicians' attitudes and behavior and the quality of their communication regarding drug–drug interaction guidelines and management.

Patient characteristics may contribute to noncompliance as well, but our finding of a higher probability of noncompliance for some patient variables, such as male sex, older age, and polypharmacy, is hard to explain. We would have expected more vigilance concerning this drug therapy–related problem in elderly patients with complex pharmacotherapy and being at higher risk. Concerning polypharmacy, a similar finding has been reported by Halkin et al.[16] in a study about preventing drug interactions. The paradox between what was expected and what was found regarding the relationship between intervention and risk factor needs further exploration. A similar paradox has been described elsewhere as the treatment–risk paradox concerning the relative undertreatment with lipid-lowering therapy of high-risk elderly patients.[17] In another study, concerning the relative undertreatment of heart failure patients at highest risk, it has been described as the risk–treatment mismatch.[18]

LIMITATIONS OF THE STUDY

First, the participating pharmacies constituted a voluntary sample, which may have resulted in a positive selection bias concerning the performance of pharmacies. The participating pharmacies all used the Pharmacom operating system, which is used by about 45% of Dutch pharmacies. The guidelines for this system are produced by the Health Base Foundation, which was described in the Methods section. The other Dutch pharmacies use other software programs, but all use the guideline system produced and maintained by another working group not described in this article. Therefore, there is the problem concerning a potential issue of reduced external validity concerning all Dutch pharmacies, but we have no information suggesting a lower or higher quality of pharmacies using the Pharmacom system. Secondly, it may be possible that some drug–drug interaction alerts were not selected or reported. Pharmacists were free to extract data every week, send them to the research center, and finally fill in and return the questionnaires. The burden of a high workload as a consequence of participation in this research project and/or in the pharmacy and the holiday season in the Netherlands resulted in a varied participation of pharma-

cies (range 1–17 drug–drug interaction alerts per pharmacy). In other words, some pharmacies may have affected the results more than others. A certain—to our opinion, low—degree of recall bias should not be ignored. It is well known that Dutch pharmacies document the management of a drug–drug interaction and other alerts, for instance, on prescription papers. Pharmacies using the Pharmacom system have an electronic documentation system in which the management of a drug–drug interaction can be described as well. Repeated testing could have influenced pharmacy management of drug–drug interactions. The frequency of most of the included drug–drug interactions, however, is low; only for some was a considerable number found. However, the average number of returned questionnaires was 5 per pharmacy (range 1–17). In combination with a study period of 3 months, we consider this issue to be a minor limitation. A certain degree of underreporting is also possible, because over-the-counter drugs, such as St John's wort, are seldom recorded in Dutch pharmacies and thus will not contribute to drug–drug interaction alerts. Nevertheless, this drug–drug interaction was included since all criteria were fulfilled. However, there is a low risk of not detecting drug–drug interactions because of a low degree of fragmented prescription filling in the Netherlands.[19] Dutch patients are in general loyal to one pharmacy, leading to rather complete medication records. Another limitation is the fact that the compliance rates are partly influenced by the ultimate decision made by the prescriber. In that way, pharmacies' compliance was not solely assessed. However, as described above, in only 22.5% of the cases was the drug–drug interaction problem presented to the prescriber. Finally, in this cohort a relatively low occurrence was found for several drug–drug interactions, meaning that the estimation of compliance rates for these drug–drug interactions is less accurate.

Conclusions

Overall compliance with Dutch guidelines for the management of drug-drug interactions was about 70%, with large differences between the various drug–drug interactions. Male sex, oldest age, and polypharmacy (>7 medications) were associated with a higher probability for noncompliance. Some prescriber-related variables had no significant influence on guideline compliance. Substitution of one of the involved agents, recommended for most of the drug–drug interactions, was executed in a minority of cases. The outcome of interaction management, such as substitution, dose reduction, or temporary stop of one of the agents, was frequently inconsistent with the guideline. Compliance rates were partly influenced by the ultimate decision made by the prescriber. In that way, pharmacies' compliance was not solely assessed. However, in only 22.5% of the cases was the drug–drug interaction problem presented to the prescriber. Further research into underlying reasons for noncompliance is warranted, such as the relationship between pharmacist and prescriber in this context.

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Obediencia a las Recomendaciones Nacionales para Gestionar las Interacciones Farmacológicas en las Farmacias Comunitarias Holandesas

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EXTRACTO

ANTECEDENTES: Los farmacéuticos contribuyen a la detección y prevención de problemas relacionados con los medicamentos, como las interacciones farmacológicas (IF). No existe mucha información sobre la obediencia a las recomendaciones para gestionar las alertas de IF.

OBJETIVOS: Cuantificar la obediencia de las farmacias comunitarias a las recomendaciones holandesas para gestionar las IF y determinar los factores relacionados con el paciente y con el facultativo que conllevan a la desobediencia.

MÉTODOS: En el estudio se incluyeron 16 IF clínicamente relevantes seleccionadas según ciertos criterios descritos. Desde junio–agosto de 2005, farmacias holandesas (n = 149) recopilaron las alertas observadas en la atención diaria al paciente dirigida especialmente a estas interacciones, junto con la información relacionada con el paciente, con la propia alerta, con el facultativo, y la gestión de la alerta. Para cuantificar la desobediencia, se comparó la gestión llevada a cabo por la farmacia con la dictada por las recomendaciones nacionales.

RESULTADOS: La obediencia global a las recomendaciones fue del 69.3% (n = 423) con grandes diferencias entre las distintas IF. El sexo masculino, (OR 2.25; IC de 95% 1.52 y 3.31), la mayor edad (>75 años) (OR 1.97; IC de 95% 1.03 y 3.75), y la politerapia (>7 medicaciones) (OR 2.35; IC de 95% 1.46 y 3.80) se asociaron con mayor probabilidad de desobediencia a las recomendaciones. Las variables relacionadas con el facultativo no mostraron ninguna influencia significativa sobre esta obediencia. Sólo en la menor parte de los casos se llevó a cabo la sustitución de uno de los fármacos implicados, medida recomendada para la mayoría de las IF. Frecuentemente, el desenlace de la gestión de la interacción, como la sustitución de un medicamento, la reducción de la dosis o la interrupción temporal de uno de los medicamentos, no coincidía con las recomendaciones. Las tasas de obediencia estaban determinadas en parte por la decisión final que tomaba el facultativo. En este sentido, la obediencia de las farmacias no se valoró en solitario. No obstante, sólo se presentó el problema de IF al facultativo en el 22.5% de los casos.

CONCLUSIONES: La desobediencia a las recomendaciones holandesas es común en las farmacias comunitarias. Se deben estudiar con mayor profundidad las razones subyacentes de esta desobediencia, como la relación entre el farmacéutico y el facultativo en este contexto.

Traducido por Violeta Lopez Sanchez

Conformité des Pharmaciens aux Lignes Directrices sur les Interactions Médicamenteuses

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RÉSUMÉ

MISE EN CONTEXTE: Les pharmaciens contribuent à la détection et à la prévention des problèmes reliés aux médicaments incluant les interactions médicamenteuses (IM). Il y a peu d'évidence sur le respect par les pharmaciens des lignes directrices portant sur la gestion des IM.

OBJECTIFS: Mesurer le respect par les pharmaciens communautaires en Hollande de lignes directrices sur la gestion des IM et déterminer les facteurs reliés aux patients et aux prescripteurs pouvant influencer le non-respect des lignes directrices.

MÉTHODES: Seize IM cliniquement significatives ont été incluses dans une étude réalisée selon certains critères. De juin–août 2005, les pharmaciens ont émis des alertes signalant la présence de ces interactions et donnant de l'information aux patients et prescripteurs sur la conduite à prendre. La conformité a été mesurée en comparant les actions prises aux lignes directrices.

RÉSULTATS: Dans l'ensemble, les règles ont été respectées dans 69,3% des cas (n = 423). Les patients de sexe masculin (rapport de cotes [RC]: 2.25; IC 95% 1.52 à 3.31), d'âge plus élevé (>75 ans) (RC 1.97; IC 95% 1.03 à 3.75), et avec une polypharmacie (>7 médicaments) (RC 2.35; IC 95% 1.46 à 3.80) ont été associés à risque plus élevé de nonconformité aux règles. Les variables reliés au prescripteur n'ont pas démontré d'influence sur les résultats. La substitution d'un des médicaments impliqués, recommandée dans la plupart des IM, n'a été exécutée que dans une minorité des cas. Les gestes posés tels que la substitution, la réduction de la dose, l'arrêt temporaire d'un des médicaments étaient fréquemment non en conformité avec les lignes directrices. Le taux de conformité était influencé par la décision ultime du prescripteur, ce qui a affecté le taux de conformité en pharmacie. Cependant, seulement 22.5% des cas d'IM ont été présentés au prescripteur.

CONCLUSIONS: La nonconformité aux lignes directrices portant sur les IM est courante dans les pharmacies communautaires en Hollande. D'autres études sont nécessaires afin de comprendre les causes sous-jacentes, notamment la relation entre le prescripteur et le pharmacien dans ce contexte précis.

Traduit par Nicolas Paquette-Lamontagne