Original Research

Management of drug interactions with beta-blockers: continuing education has a short-term impact

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ABSTRACT[*]

There is a lack of clear guidelines regarding the management of drug-drug interactions.

Objective: To assess the impact of an educational intervention on the management of drug interactions with beta-blockers.

Methods: The study had a controlled before-and-after design. The intervention group (n=10 pharmacies) received a continuing education course and guidelines on the management of drug interactions with beta-blockers. The control group (n=10 pharmacies) received no intervention. Pharmacy students and staff of internship pharmacies participated in this study. Before and after the intervention, students registered interactions with beta-blockers during two weeks. Information was obtained on drug information of the beta-blocker and the interacting drug, patient's demographics, and the mode of transaction.

Results: A total number of 288 interactions were detected during both study periods. Most beta-blockers causing an interaction were prescribed for hypertension, and interacted with hypoglycemic agents, NSAIDs, or beta2-agonists. Pharmacists' intervention rate was low (14% in the pre-test compared to 39% in the post-test), but increased significantly in the post-test in the intervention group. Reasons for overriding the interaction included limited clinical relevance, refill prescriptions, not being aware of the interaction, and communication problems with the prescriber.

Conclusion: An interactive continuing education course, during which practice-oriented guidelines were offered, affected pharmacists' short-term behavior at the counter in dealing with interactions of beta-blockers. Continuing education plays a role in raising pharmacists' awareness and responsibility towards the detection and management of drug interactions in the pharmacy.

Keywords: Drug Interactions. Pharmacy continuing education. Pharmacists. Belgium.

RESUMEN

Existe una carencia de guías claras sobre el manejo de las interacciones medicamento-medicamento.

Objetivo: Evaluar el impacto de una intervención educativa sobre la gestión de las interacciones medicamentosas con beta-bloqueantes.

Métodos: El estudio tiene un diseño controlado antes-después. El grupo intervención (n=10 farmacias) recibió un curso de formación continuada y guías sobre la gestión de las interacciones con beta-bloqueantes. El grupo control (n=10 farmacias) no recibió intervención. Los estudiantes de farmacia y el personal interno de las farmacias participaron en este estudio. Antes y después de la intervención, los estudiantes registraron las interacciones con beta-bloqueantes durante dos semanas. Se obtuvo información sobre la información del beta-bloqueante y el medicamento interaccionante, la demografía del paciente, y el modo de la transacción.

Resultados: Se detectaron un total de 288 interacciones durante ambos periodos de estudio. La mayoría de los beta-bloqueantes que producían interacciones fueron prescritos para hipertensión, e interaccionaban con hipoglucémiantes, AINE, o beta2-agonistas. La tasa de intervención de los farmacéuticos fue baja (14% en el pre-test contra 39% en el post-test), pero aumentó significativamente en el post-test del grupo intervención. Las razones para ignorar la interacción incluían la limitada relevancia clínica, las prescripciones de repetición, no ser consciente de la interacción, y problemas de comunicación con el prescriptor.

Conclusión: Un curso de formación continuada interactivo, durante el cual se ofrecieron guías de práctica, afectó a corto plazo la actitud de los farmacéuticos en el mostrador al enfrentarse a interacciones de beta-bloqueantes. La formación continuada juega un papel importante en elevar el conocimiento de los farmacéuticos y la responsabilidad hacia la detección y gestión de las interacciones medicamentosas en la farmacia.

Palabras clave: Interacciones medicamentosas. Formación continuada de farmacia. Farmacéuticos. Bélgica.

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(English)

INTRODUCTION

Drug-related problems (DRPs) are defined by the Pharmaceutical Care Network Europe (PCNE) as

"events or circumstances involving drug therapy that actually or potentially interfere with desired health outcomes".[1] DRPs are associated with significant morbidity, impaired quality of life, mortality, and are a primary driver of hospital admissions and health care costs. In a recent study in England, it was estimated that up to 6.5% of hospital admissions was due to adverse drug events, over 70% of those being preventable. The annual cost of these hospital admissions was estimated at 706 million euros (847 million US dollars) (2002).[2]

Community pharmacists can contribute to the prevention and identification of DRPs, with pharmacists' interventions being associated with reduced hospital admissions,[3] and prevention of possible patient harm.[4-6] In a study of Currie and colleagues, the effect of a training program on the detection of DRPs was investigated. The training program led to an increase in the detection of DRPs. However, the study did not focus on better DRP management as a result of the training program.[7]

The PCNE classification system identifies a number of categories of DRPs, one of which is drug interactions.[1] Delphi+ is a commonly used program for detecting drug-drug interactions in community pharmacies in Belgium. The program is based on the ABDA's (German Association of Community Pharmacists) drug interaction database, which has been adapted to the medicines available on the Belgian market. It screens interactions based on the relevance criteria documentation and severity. Four categories of severity are distinguished: very severe, severe, less important, and insignificant. Pharmacists are advised to adjust the program so that only the first two categories are activated. As a result, work at the counter will not unnecessarily be delayed by focusing on less significant drug interactions. The documentation status also exists of four categories: causality evidenced, suspected, unlikely, and unable to pronounce upon. Only in the first two cases, an interaction sign will be shown.

An issue in the management of drug interactions is the overwhelming amount of information available to pharmacists.[8] This problem is often found in software programs designed for pharmacy practice. In their study on the use of the drug surveillance program Delphi+, Leemans & Laekeman (1994) found that 32% of pharmacists hardly ever used the interaction screening part of the program (n=164). The main reason was the program being time consuming due to the lack of gradation in importance and relevance of interactions.[9] Hansten came to a similar conclusion through informal polls of pharmacists around the United States.[8] Bates argues that pharmacists may be bombarded by so many interaction reports that they grow accustomed to skipping through them rapidly.[10] Finally, McDonald described the phenomenon that individuals who are given too much information will stop paying attention to it, with potentially disastrous consequences.[11]

The appropriate management of drug interactions also depends on the knowledge of the health care practitioner. Outside the physicians's cabinet, the pharmacist is the last line of defense to protect the patient from prescribing errors. But can (s)he fulfill that role? Westerlund found that the educational level of the pharmacy practitioner was a key determinant for the detection of DRPs[12] and Hansten concluded that the drug interaction knowledge of health care providers has to be improved.[8] Leape and colleagues identified failure in the dissemination of drug knowledge as being the most common cause of drug interaction errors.[13] In a study of Cavuto and colleagues, 16 (32%) of 50 pharmacies filled two prescriptions -one with erythromycin and the other with terfenadin- without comment, although 48 of the 50 pharmacies used computer programs designed to prevent drug interactions.[14] In reply to this article, Bates argues that part of the problem may be with the computer systems.[10] However, we should not forget that this interaction is one of the few potentially fatal interactions and that pharmacists should have the knowledge to handle this problem rather than rely completely on imperfect software programs.

Clearly, there is a need to provide community pharmacists with education, practice-oriented tools, and instructions to manage drug interaction problems in the pharmacy.

METHODS

During two weeks all drug interactions were documented in six community pharmacies, located in different geographical areas in Belgium, in order to identify the drug interactions that occurred most frequently. Drug interactions with beta-blockers appeared to be the most common ones (85 out of a total of 307 interactions). This finding is consistent with other researchers' results.[15,16]

Six beta-blocker drug interactions, which the Delphi + software program indicated as severe or very severe were selected for the study. Those were interactions of beta-blockers with hypoglycemic agents, beta-agonists, Ca-channel blockers, ergot alkaloids, NSAIDS and rizatriptan. Because there is no consensus on the clinical relevance of drug interactions with beta-blockers,[17] different drug information sources were consulted to develop practice-oriented guidelines.[18-20] Each guideline consisted of a flowchart detailing the interaction problem and the ways of dealing with the drug interaction, i.e. mode of transaction. With respect to the mode of transaction, a distinction was made between the first time the two drugs are combined, and renewal of the drug combination. Also mentioned on the flowcharts were patients' risk factors that could increase the severity of the interaction, situations in which the pharmacist should contact the physician, the suggestion for registration in the computer of the mode of transaction, and for follow-up of the patient (Figure 1). Additional information regarding mechanism of action, clinical significance of the interaction, and mode of transaction were provided in a separate document.
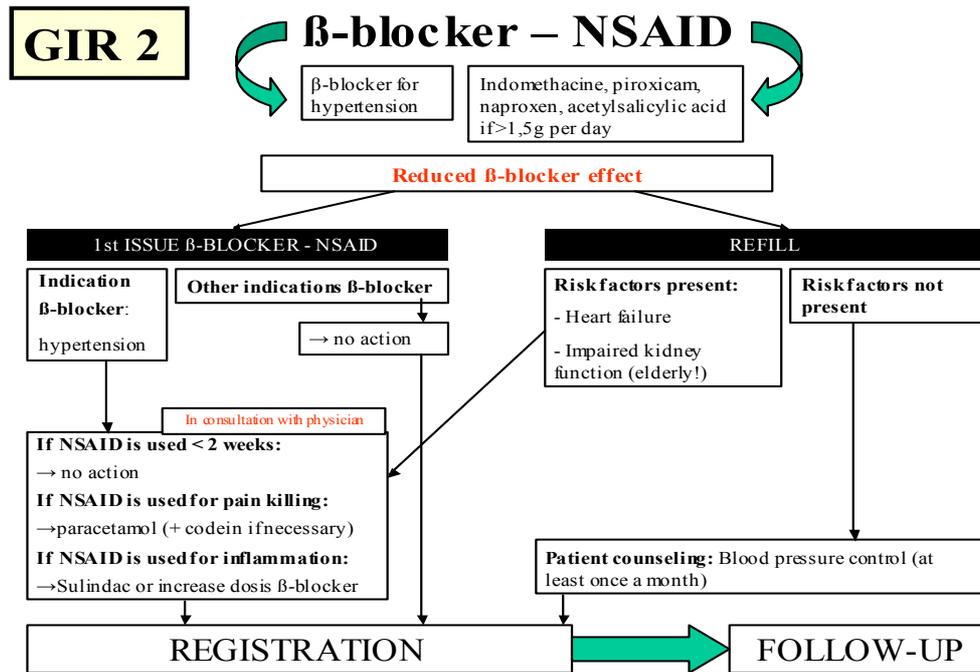
GIR 2 — ß-blocker – NSAID

β-blocker for hypertension	Indomethacine, piroxicam, naproxen, acetylsalicylic acid if >1,5g per day

Reduced ß-blocker effect

1st ISSUE ß-BLOCKER - NSAID

Indication ß-blocker: hypertension

Other indications ß-blocker → no action

REFILL

Risk factors present:
- Heart failure
- Impaired kidney function (elderly!)

Risk factors not present

In consultation with physician

If NSAID is used < 2 weeks:
→ no action
If NSAID is used for pain killing:
→ paracetamol (+ codein if necessary)
If NSAID is used for inflammation:
→ Sulindac or increase dosis ß-blocker

Patient counseling: Blood pressure control (at least once a month)

REGISTRATION ➡ **FOLLOW-UP**

Figure 1. Flowchart of drug interaction beta-blocker – NSAID

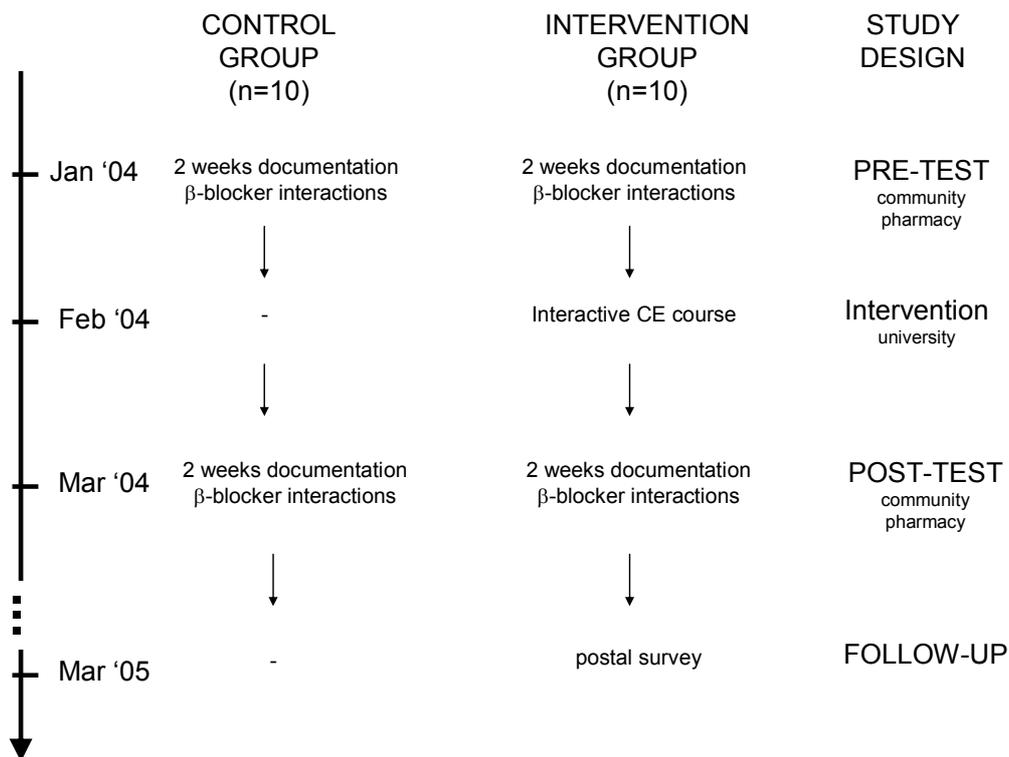|	CONTROL GROUP (n=10)	INTERVENTION GROUP (n=10)	STUDY DESIGN
Jan '04	2 weeks documentation β-blocker interactions	2 weeks documentation β-blocker interactions	PRE-TEST community pharmacy
Feb '04	-	Interactive CE course	Intervention university
Mar '04	2 weeks documentation β-blocker interactions	2 weeks documentation β-blocker interactions	POST-TEST community pharmacy
Mar '05	-	postal survey	FOLLOW-UP

Figure 2. Study design

All final year pharmacy students, who were in their internship period, were sent a letter to probe their interest in the study. Students could only participate if their internship mentors were also willing to co-operate and if at least one person from the pharmacy could attend the intervention session in February 2004. Ten students together with their internship pharmacy were willing to participate in the study. An equal number of students from another university together with their internship pharmacies formed the control group. No incentives

were provided for the pharmacies to participate in this study.

The study had a controlled before-and-after design and explored how the management of drug interactions evolved in the intervention and control group after the intervention group had been exposed to an interactive CE course (Figure 2). Prior to the study, both student groups were informed about the purpose of the study and were given instructions on how they had to document drug interactions.

In January 2004, the two student groups registered interactions of beta-blockers with NSAIDs, beta-agonists, hypoglycemic agents, Ca-channel blockers, ergot alkaloids, and rizatriptan that occurred in their internship pharmacy during two weeks. A list was provided with all the brand names of the beta-blockers (orally administrated as well as eye drops), and the drugs listed above for which the interaction had to be controlled. Students controlled every prescription that contained one or more drugs from the list. In case there was only one drug on the prescription, the medication history of the patient was checked to see whether the patient was currently taking a drug that could possibly interact. Each interaction was registered on a separate form and was discussed with the pharmacist who had filled that prescription.

The topics to be completed on the form were related to drug information of the beta-blocker and the interacting drug, patient's demographic features, and the mode of transaction. In the drug information category, information had to be provided on dose, posology, indication, whether the two drugs were prescribed by the same physician, and whether the drug was on the prescription or in the medication history of the patient. In the patient information section, students registered the age of the patient, and the number of medicines that the patient was currently taking, apart from the two interacting drugs. Patients themselves were not interviewed, nor were their names recorded on the forms. Finally, with respect to the mode of transaction, students had to indicate how the pharmacists who filled that prescription had dealt with the reported drug interaction. Possible transactions were: no intervention, counseling with patient, contact with physician, and other actions which were to be specified. These items were not mutually exclusive. In this part, the student also reported what exactly was changed in case of therapy adjustment as well as the pharmacist's motivation for the chosen transaction.

In February 2004, the intervention group, consisting of the students as well as the internship pharmacy staff, took part in the intervention. The internship mentors were invited to attend the session with as many staff of their pharmacy as possible (pharmacists as well as pharmacy technicians). During the intervention session, the students as well as the pharmacy staff were trained to use the developed drug interaction guidelines in the pharmacy. After an introductory lecture, the use of the guidelines was practiced in small groups. The control group received no training.

Post-test. Three weeks after the interactive session, students in the intervention and control group registered all interactions of beta-blockers during two weeks following the same methodology as in the pre-test.

One year after the study, pharmacists who participated in the intervention group were sent a questionnaire. This survey contained questions on the information retained from the interactive session, and the use of the developed flowcharts.

Chi square analysis at a 0.05 level of significance, was used to analyze statistical differences between pre-test and post-test and between the intervention and the control group.

RESULTS

A total number of 288 interactions were detected during both study periods. In the intervention group, 88 interactions were detected in the pre-test and 56 interactions in the post-test. In the control group, 67 interactions were registered in the pre-test and 77 interactions in the post-test. The mean number of prescriptions per day per pharmacy was 75 (SD=34), resulting in an estimated incidence of beta-blocker interactions of 1.92%. Of all 288 interactions, 35.4% occurred with anti-hypoglycemic agents, 31.9% with NSAIDs, 21.5% with beta2-agonists, 9.4% with Ca-channel blockers, 1.4% with ergotamines, and 0.3% with rizatriptan. No difference was seen between pre-test and post-test or between intervention and control group. Of all detected interactions, 84.5% of beta-blockers were found on the prescription, compared to 15.5% in the medication history of the patient. Table 1 gives an overview of the different indications for which the beta-blocker was prescribed. The interacting drug was found on the prescription in 56.7% of interactions, and in the medication history in 43.3% of interactions.

Table 1. Indications of the beta-blockers causing an interaction	
Indication	% (n=288)
Hypertension	64.6
Glaucoma	10.8
Heart failure	4.2
Angor	1.4
Migraine	0.7
Other	3.8
Did not know, no answer	14.6

Sixty-six percent of detected drug interactions occurred in patients aged between 60 and 80. Patients were aged between 40 and 60 in 18.9% of interactions, patients were older than 80 years in 12% of interactions, and patients were younger than 40 years in 3.2% of interactions. On average, patients took 3.73 (SD=2.25) medicines in addition to the two that caused the interaction. In 85% of all detected interactions, the prescriber of both interacting drugs was the same, whereas in 15% of interactions the interacting drugs were prescribed by different physicians.

In total, 86% of detected interactions were not acted upon in the pre-test (Table 2). In the intervention group this number decreased from 89% in the pre-

test to 27% in the post-test (p<0.001), whereas in the control group the number of untreated interactions slightly increased in the post-test (p=0.171). In none of the reported interactions, the therapy was immediately adjusted on the initiative of the pharmacist or after consultation of the physician. The category "other actions" mainly included typing a note in the patient's record so that the pharmacist would be aware of the interaction and that patients would be given advice about the interaction next time they come to the pharmacy.

In the intervention group, pharmacists' awareness of interactions increased. They failed to detect an interaction in 2% of cases in the post-test,

compared to 25% in the pre-test (p<0.001). In the post-test, the intervention group more often justified their transactions by minimizing the problem. Reasons were, among other things, that they had evaluated the patient's risk factors for the interaction, that the physician was aware of the interaction, that the pharmacist estimated the interaction was not clinically relevant, that the patient had taken this combination before, or that actions had already been taken to counteract the interaction. In the post-test, the intervention group more often reported communication problems with physicians compared to the pre-test (p<0.001) and the control group (p<0.001).

Table 2. Mode of transaction		Group		
	% Total (n=144)	% Intervention group (n=88)	% Control group (n=67)	Chi square
Pre-test				
No intervention	86	89	84	
Patient counseled	10	10	9	p=0.128
Doctor contacted	4	1	7	
Other actions	0	0	0	
	% Total (n=144)	% Intervention group (n=56)	% Control group (n=77)	
Post-test				
No intervention	61	27	87	
Patient counseled	24	39	12	p<0.001
Doctor contacted	9	20	1	
Other actions	6	14	0	
	Chi square	p<0.001	p=0.171	

Table 3. Justification for overriding the interaction		Group		
	% Total (n=144)	% Intervention group (n=88)	% Control group (n=67)	Chi square
Pre-test				
Minimizing the problem	50	49	52	
Communication problem with doctor	2	2	2	p=0.949
Did not know/see the interaction	25	25	25	
No answer	23	24	21	
	% Total (n=144)	% Intervention group (n=56)	% Control group (n=77)	
Post-test				
Minimizing the problem	66	75	59	
Communication problem with doctor	7	14	1	p=0.001
Did not know/see the interaction	9	2	15	
No answer	18	9	25	
	Chi square	p<0.001	p=0.434	

Of the participants of the CE course (15 pharmacists, no pharmacy technicians), ten returned the follow-up questionnaire, which was sent one year later to the pharmacists in the intervention group (Table 4). When asked to recall the CE course, pharmacists mainly mentioned issues related to the setting and the course of the CE session. Six of the ten responders did not use the developed guidelines anymore. Of those, three responders mentioned that the guidelines should be integrated with the software programs.

DISCUSSION

This study aimed to evaluate the short-term effects of an interactive CE course on the management of beta-blocker drug interactions on practice improvement of community pharmacists. The CE course had an effect on the intervention rate, the mode of transaction, and knowledge of drug interactions with beta-blockers.

The majority of detected interactions were caused by beta-blockers that are prescribed for hypertension. This information on the indication of

the beta-blocker is important to evaluate the clinical significance of some interactions. For example, it is well established that the pharmacodynamic drug interaction beta-blocker – NSAID is particularly significant when the beta-blocker is administered for hypertension.[20] In almost 15% of detected drug interactions in our study, the student or the pharmacist was not aware of the purpose of the beta-blocker. In line with this result, a European study on DRPs identified lack of knowledge of the aim of the drug as the most common DRP.[6] Other researchers discern that community pharmacists

have limited access to decision-relevant patient information beyond that which can be collected from the patient.[4,21] In this respect, Finland requires physicians to write the purpose of the medication on the prescription,[22] and provides open access for both prescribing and dispensing parties to the same patient database.[15] Rupp concluded that, in expectation of this open access, communication and collaboration between prescribers and pharmacists is a prerequisite in the proper management of DRPs.[4]

Table 4. Follow-up of the pharmacists who participated in the interactive session	
What do you remember of the CE course on drug interactions with β-blockers?	n (n=10)
- Little, nothing, no answer	4
- Setting (nice place, contact with colleagues,…)	4
- Flowcharts received	3
- Description of the course of the evening	4
That evening, did you learn something about drug interactions with β-blockers? If so, what exactly did you learn?	n (n=10)
- No answer	4
- The importance and occurrence of drug interactions with β- blockers	4
- Drug interaction of β-blockers with NSAIDs	2
- Occurrence of drug interactions with β-blocker eye drops	1
- Everything I know now about drug interactions with β-blockers, I learned that evening	1
Do you still use the flowcharts? If so, how often?	n (n=10)
- No answer	2
- I don't use them anymore	6
- monthly	1
- Less than monthly	1
Why is it that you do not use the flowcharts anymore?	n (n=6)
- No answer	2
- Lack of time	2
- Should be integrated in the software	3

Various studies have described difficult pharmacist-prescriber contacts as a barrier to optimal provision of patient care by pharmacists.[4,22,23] In our study, communication with prescribers was only occasionally reported as a problem, albeit that the frequency of communication problems with physicians significantly increased in the intervention group after the CE course. It is unclear why this occurred and this issue requires further investigation. One possible explanation could be that the frequency of prescriber contacts was higher in the post-test, resulting in a proportional increase in communication problems.

Following the CE course in the intervention group, patients were more often counseled and physicians were more often contacted to discuss the problem. However, in almost 30% of cases, pharmacists still preferred not to undertake any actions. The most important reason was that they minimized the interaction problem because they did not estimate the interaction to be clinically relevant or because the prescriptions were refills. These reasons could be part of the explanation why in none of the cases the therapy was adjusted, even when the prescriber had been contacted. Prescribers, in turn, may have similar problems as pharmacists in the management of drug interactions. Lack of knowledge, drug interaction screening programs generating too many

alerts and being too time consuming, doubts on the clinical relevance, and patients having tolerated the drug combination in the past, have been found to be reasons for overriding drug interactions in the physicians' cabinet.[24-28] To overcome some of these factors, Spina and colleagues have suggested that drug surveillance programs should include mandatory alerts for life-threatening DRPs of which the prescriber may not be aware, and that the programs should be more interactive and flexible so that prescribers can tailor those programs to their perceived needs.[28] In accordance with our findings, this suggestion could be extended to pharmacists' drug surveillance programs.

The CE course had an effect on the detection rate of drug interactions. The 'did not know/see the interaction' reason for not intervening in the interaction decreased to 2% in the intervention group following the CE course. The reason why pharmacists failed to see the interaction may be because some pharmacists in this study did not have drug surveillance software, or did not use those programs properly, and because pharmacists' knowledge of drug interactions may be inadequate. Therefore, CE courses on drug interactions like the one that we provided, play a key role in updating pharmacists' knowledge and in raising their responsibility of preventing DRPs. Simultaneously,

pharmacies could be obliged to use medication surveillance screening programs, which is already the case in for example the Netherlands.[29] However, those programs will never be able to replace pharmacists' reasoning and decision making. Pharmacists, as drug experts, should take up their responsibility of detecting and preventing DRPs, if they wish to claim a role in DRP assessment.[30]

The increased knowledge following the interactive CE course did not appear to have a long-lasting effect. The follow-up survey revealed that pharmacists did not remember much of the CE course. One pharmacist said that she learned everything she knew about drug interactions during that evening. It could be that graduate education did not draw enough attention to DRPs and that therefore a single CE course was not enough to bring pharmacists' knowledge about drug interactions with beta-blockers up to date. We did not investigate whether pharmacists' improvements in the management of drug interactions with beta-blockers were sustained over time. Given the limited knowledge retained by pharmacists over time and the fact that more than half of respondents did not use the guidelines anymore, we expect little sustained practice changes. In the literature, there used to exist little evidence on the impact of CE on practice improvement.[31] However, recent studies suggest that long-lasting practice improvement may be obtained through curriculum-based CE courses, long-term courses involving the whole pharmacy team, or a combination of interactive CE courses with on-site performance feedback.[32-34] These studies may be inspiring for further research on long-lasting practice improvement in the management of drug interactions.

This study has several limitations. First, data were collected in internship pharmacies. It could be that internship mentor pharmacists are more receptive of continuing education courses and interventions to effect practice improvement than the average pharmacist, which could have led to an overestimation of our results. Second, pharmacists were not randomly assigned to the intervention or control group because of the risk of exchanging information between students of the same university and pharmacists from the same region.

CONCLUSION

A single CE course on management of beta-blocker interactions had a positive short-term effect on pharmacists' awareness, evaluation of clinical relevance, contact with prescribers, and patient counseling. Further research is needed to develop CE programs that facilitate sustained practice improvement in the management of drug interactions.

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