

ARTICLE

Effect of Misalignment between Hospital and Provincial Formularies on Medication Discrepancies at Discharge: PPITS (Proton Pump Inhibitor Therapeutic Substitution) Study

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ABSTRACT

Background: Medication discrepancies may occur on admission, transfer, or discharge from hospital. Therapeutic interchange within a drug class is a common practice in hospitals, and orders for specific proton pump inhibitors (PPIs) are often substituted with the hospital's formulary PPI through therapeutic interchange protocols. Rabeprazole is the PPI on the formulary of the British Columbia PharmaCare program. However, different PPIs may appear on the formularies of the province's hospitals. This misalignment and use of therapeutic interchange may lead to increased rates of medication discrepancies at the time of discharge.

Objective: To evaluate the effect of formulary misalignment for PPIs between St Paul's Hospital in Vancouver and the British Columbia PharmaCare program and use of therapeutic interchange on the occurrence of medication discrepancies at discharge.

Methods: A cohort chart review was performed to compare discharge discrepancy rates for PPI orders between 2 periods: June 2006 to June 2008, when the same PPI appeared on the hospital and provincial formularies, and July 2008 to July 2010, when the designated PPIs differed between the hospital and provincial formularies. Data for the first study period were used to establish the baseline discharge discrepancy rate, and data for the later period represented the discharge discrepancy rate in the presence of misalignment between the hospital and PharmaCare formularies.

Results: The discharge discrepancy rate for PPIs was 27.3% (24/88) when the 2 formularies were aligned and 49.1% (81/165) when the formularies were misaligned. This represents an absolute increase of 21.8 percentage points in the risk of discharge discrepancies (95% confidence interval 9.8–33.9 percentage points; $p < 0.001$) when the hospital and provincial formularies were misaligned and the hospital's therapeutic interchange protocol was used.

Conclusions: Misalignment between the PPIs specified in the hospital and provincial formularies, combined with use of therapeutic interchange, was associated with a significant increase in medication discrepancies at discharge.

RÉSUMÉ

Contexte : Les divergences de médication peuvent survenir à l'admission, au transfert ou au congé du patient d'un hôpital. La substitution thérapeutique au sein d'une classe de médicaments est une pratique courante dans les hôpitaux et les ordonnances pour des inhibiteurs de la pompe à protons (IPP) particuliers sont souvent modifiées pour leur substituer l'IPP inscrit au formulaire de l'hôpital par le truchement de protocoles de substitution thérapeutique. Le rabeprazole est le seul IPP inscrit sur la liste de médicaments du programme d'assurance-médicaments PharmaCare de la Colombie-Britannique. Toutefois, différents IPP peuvent apparaître dans les formulaires des hôpitaux de cette province. Ce défaut d'harmonisation et le recours à la substitution thérapeutique peuvent se traduire par des taux accrus de divergence de médication au moment du congé du patient de l'hôpital.

Objective : Évaluer l'incidence du décalage des IPP entre le formulaire de l'Hôpital Saint-Paul à Vancouver et la liste de médicaments du programme d'assurance-médicaments PharmaCare de la Colombie-Britannique et le recours à la substitution thérapeutique sur la survenue des divergences de médication lors du congé du patient de l'hôpital.

Méthodes : Une analyse rétrospective des dossiers médicaux a été réalisée afin de comparer les taux de divergence dans les ordonnances d'IPP lors du congé de deux cohortes de patients au cours des périodes : de juin 2006 à juin 2008, lorsque le même IPP était inscrit au formulaire de l'hôpital et à la liste de médicaments provinciale, et de juillet 2008 à juillet 2010, lorsque les IPP inscrits au formulaire hospitalier et à la liste de médicaments provinciale différaient. Les données pour la première période ont été utilisées pour établir le taux initial de divergence au congé, et celles de la deuxième période, pour représenter le taux de divergence au congé en présence du décalage entre le formulaire de l'hôpital et la liste de médicaments provinciale.

Résultats : Le taux de divergence au congé pour ce qui est des IPP était de 27,3 % (24/88) lorsque le formulaire hospitalier était harmonisé à la liste de médicaments provinciale et de 49,1 % (81/165) lorsqu'ils différaient. Cela représente une augmentation absolue de 21,8 points de pourcentage du risque de divergence au congé (intervalle de confiance à 95 %, 9,8 – 33,9 points de pourcentage; $p < 0,001$) en présence du décalage entre le formulaire de l'hôpital et la liste de médicaments provinciale et du recours au protocole de substitution thérapeutique de l'hôpital.

Key words: therapeutic interchange, discharge discrepancy, proton pump inhibitors, misalignment, hospital formulary

Conclusion : Le décalage entre les IPP inscrits au formulaire de l'hôpital et à la liste de médicaments provinciale, conjugué au recours à la substitution thérapeutique, a été associé à une augmentation significative des divergences de médication au congé du patient de l'hôpital.

Mots clés : substitution thérapeutique, écarts lors du congé du patient de l'hôpital, inhibiteurs de la pompe à proton, non-harmonisation, formulaire d'hôpital

[Traduction par l'éditeur]

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INTRODUCTION

Patient safety, including minimization of drug-related errors, has become a priority within the Canadian health care system. Adverse drug events are unintended injuries resulting from medical interventions related to the use of medications.¹ Errors in the ordering, dispensing, or administration of a medication can result in such adverse events and may occur at any transition in patient care during the hospital stay (admission, transfer, or discharge).^{1,2} Discharge discrepancies, defined as differences between the medications a patient is taking at the time of discharge and those the patient was taking before admission, may be intentional or unintentional, with the latter being considered medication errors.^{2,3} In one study, 70% of patients had at least one unintentional discrepancy at discharge from hospital.⁴ These discharge discrepancies can lead to delays in obtaining medications after discharge, as well as patient discomfort, clinical deterioration, and potential harm because the patient lacks an understanding of changes to his or her medication regimen.⁴

Therapeutic interchange is the hospital-authorized exchange or substitution of a prescribed drug with an alternative, therapeutically equivalent drug within the same therapeutic class.⁵ Implementation of therapeutic interchange protocols has increased substantially in recent years because of expansion in the number of drugs within each therapeutic class.⁴ Proton pump inhibitors (PPIs) are a class of medications that are subject to therapeutic interchange in many hospitals.⁴ These drugs are commonly used to treat gastrointestinal reflux disease and peptic ulcer disease and for gastrointestinal prophylaxis. Six PPIs are available on the North American market: esomeprazole, lansoprazole, omeprazole, pantoprazole sodium, pantoprazole magnesium, and rabeprazole. St Paul's Hospital, in Vancouver, British Columbia, has a therapeutic interchange protocol for PPIs, whereby PPIs ordered for inpatients are substituted with one of the PPIs designated in the hospital's formulary (specifically, esomeprazole and lansoprazole, at the time this study was performed). However, during the study

period, the provincial drug program in British Columbia (PharmaCare), which provides drug coverage for all nonhospitalized residents of the province (as described below), covered only the cost of rabeprazole. Thus, the formulary PPIs used for inpatients at St Paul's Hospital (esomeprazole and lansoprazole) were not aligned with the PPI covered by BC PharmaCare (rabeprazole).

All residents of British Columbia are eligible for the BC PharmaCare program for coverage of outpatient prescription drug costs, provided the drug is listed or eligible for coverage according to the program's formulary. If a medication is not listed or eligible for PharmaCare coverage, the patient must pay the entire cost of the prescription.

Misalignment between hospital and PharmaCare formularies would lead to a change in the patient's medication regimen, from the preadmission medication (i.e., the PPI on the PharmaCare formulary) to a different, yet therapeutically equivalent medication (i.e., the PPI on the hospital formulary) during the hospital stay, through therapeutic interchange. Such a substitution might lead to a discharge discrepancy, which could result in adverse outcomes because of patients' lack of awareness of the nonclinical rationale for changing their PPI on discharge. Any confusion on the patient's part might result in compliance issues, as well as potential omission or duplication of therapy, which could ultimately lead to adverse drug events.

The purpose of this study was to evaluate the effect on medication discrepancies at discharge of formulary misalignment for PPIs between the hospital and the BC PharmaCare program and the use of therapeutic interchange during the hospital stay.

METHODS

Study Design

This retrospective study compared discrepancy rates between 2 cohorts of patients at St Paul's Hospital who received PPI therapy: those treated from June 2006 to June 2008, when the hospital formulary was aligned with the BC PharmaCare formulary, and those treated from July 2008 to July 2010,

when there was a misalignment between the hospital and PharmaCare formularies.

From June 2006 to the time of writing (late 2011), rabeprazole has been the PPI on the PharmaCare formulary. Starting on January 26, 2010, the cost of pantoprazole magnesium has also been reimbursed by PharmaCare.⁶ From June 2006 to June 2008, the PPI on the St Paul's Hospital formulary was rabeprazole. Analysis of data for this period established the baseline incidence of discharge discrepancies (i.e., when the hospital and PharmaCare formularies were aligned). From July 2008 to July 2009, the PPI on the St Paul's Hospital formulary was lansoprazole, and from August 2009 to July 2010, it was esomeprazole. Data for the period July 2008 to July 2010 represent the change in discharge discrepancy rates when there was misalignment in PPIs between the hospital and PharmaCare formularies.

Patient Selection

All patients admitted to the St Paul's Hospital inpatient cardiology wards from June 2006 until July 2010 for whom a PPI was prescribed during the hospital stay were identified through the pharmacy information system. Patients were enrolled in the study if they had been taking a PPI before admission and during the hospital stay and if a PPI had been prescribed at discharge. Patients with unknown medication history or intolerance to a particular PPI, those who were transferred out of the cardiology ward, those who died in hospital, and those who did not receive a cardiology discharge prescription for PPI were excluded. The cardiology discharge prescription is a triplicate discharge prescription form, with a carbon copy of each prescription as provided to the patient being stored in the hospital's medical records.

Outcome Measures

The primary outcome was the rate of discharge discrepancies for PPIs. A discharge discrepancy was defined as a difference between the PPI prescribed at discharge and the PPI the patient was taking at the time of admission, as a result of therapeutic interchange.

Data Collection

For all patients included in the study, the St Paul's Hospital pharmacy computer system and medical records were reviewed for demographic characteristics, length of hospital stay, PPI used before admission, PPI prescribed during the hospital stay, and PPI prescribed at discharge. The data were collected in a password-encoded Excel (Microsoft, Redmond, Washington) spreadsheet.

Statistical Analysis

Discharge discrepancy rate was analyzed using Fisher's exact test, with SPSS version 9 for Windows (IBM, Armonk, New York).

RESULTS

A total of 2408 PPI prescriptions were ordered for inpatients during the 2 study periods. Of these patients, 253 met the inclusion criteria, 88 during the period of formulary alignment and 165 during the period of formulary misalignment. Age, sex ratio, and mean length of stay were similar in the 2 groups (Table 1). The majority of enrolled patients were taking rabeprazole before admission to hospital in both periods: 52 (59%) of 88 patients during the period of alignment and 79 (48%) of 165 patients during the period of misalignment (Figure 1).

The discharge discrepancy rate for PPIs (the primary outcome) was 27.3% (24/88) during the period of formulary alignment and 49.1% (81/165) during the period of misalignment. This represents an absolute increase of 21.8 percentage points (95% confidence interval [CI] 9.8–33.9 percentage points; $p < 0.001$) in the risk of a medication discrepancy at discharge. The majority of these discharge discrepancies were caused by therapeutic substitution of the hospital's formulary PPI for the PPI ordered (discrepancy rate attributed to therapeutic substitution: 12/24 [50%] during the period of formulary alignment and 61/81 [75%] during the period of formulary misalignment).

DISCUSSION

In this study, the discharge discrepancy rate for PPIs increased after a change in the hospital formulary that resulted in misalignment with the BC PharmaCare formulary. Aside from this formulary misalignment and therapeutic interchange, no other causes for the increase in discrepancy rate could be identified. The wards were staffed by the same clinical pharmacy specialist (D.C.) during the 4-year study period, and hence medication reconciliation at discharge was performed consistently. The St Paul's Hospital PPI therapeutic interchange protocol is used frequently, and deviations from the protocol are rare. Starting January 26, 2010, BC PharmaCare reimbursed patients for pantoprazole magnesium, in addition to rabeprazole, but this would not have affected the primary outcome: the PPI on the hospital formulary was esomeprazole, so even with the addition of pantoprazole magnesium to the provincial formulary, there was still misalignment between the hospital and PharmaCare formularies.

Other researchers have reported discharge discrepancy rates ranging from 14% to 71%.^{4,7-9} This wide range may be due to differences between the studies in terms of patient populations and methods of identifying discharge discrepancies. The baseline discharge medication discrepancy rate of 27.3% during the period of formulary alignment and the increase to 49.1% during the period of formulary misalignment are consistent with the previous studies, which established that

Table 1. Demographic Characteristics of Patients

Characteristic	Period A (Formulary Alignment)	Period B (Formulary Misalignment)
No. of patients	88	165
Sex, no. (%) male	57 (65)	102 (62)
Age (mean ± SD)	68.2 ± 13.0	67.1 ± 12.0
Length of stay (days) (mean ± SD)	6.05 ± 5.75	7.43 ± 9.48

SD = standard deviation.

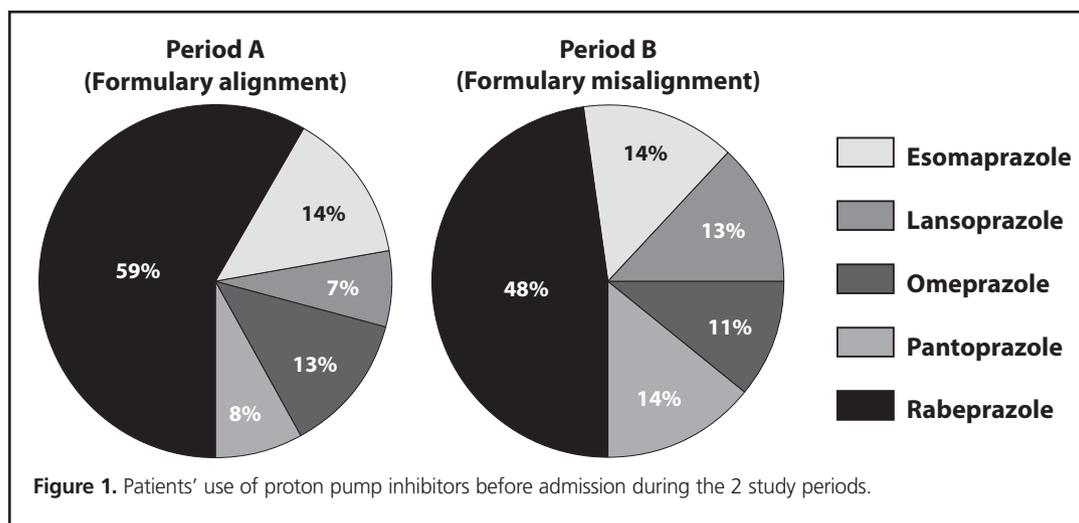


Figure 1. Patients' use of proton pump inhibitors before admission during the 2 study periods.

discharge discrepancies are prevalent. Previous studies have attributed the discrepancies to a variety of causes, such as incomplete discharge instructions, incomplete prescriptions, omission of medications, and duplication of medications.^{4,7-9} To our knowledge, this is the only study to date that has specifically investigated the role of a hospital's therapeutic interchange protocol and its influence on discharge discrepancies, with a focus on one drug class (PPIs). As well, the assessment of outcomes in this study was robust, as it was based on a carbon copy of the prescription given to each patient, rather than dictated discharge summaries or chart notes.

The retrospective nature of this study was its main limitation. Despite a span of 2 years in each study period, the number of patients was relatively small: 88 and 165 in each period, respectively. The difference in numbers was due to less widespread use of the cardiology discharge form and poorer documentation during the earlier period and improvements in these practices during the later period. As well, the study had strict inclusion and exclusion criteria, to maintain the integrity of the results. Given the retrospective nature of the study, a causal effect of therapeutic interchange on discharge discrepancies cannot be inferred, but a strong association was demonstrated.

Another limitation is the fact that the clinical effect of the discharge discrepancies on the patients is unknown. It is

possible that some patients did not obtain the medications that physicians prescribed upon hospital discharge. Alternatively, patients might have returned to using their previous supply of PPI (from before admission to hospital), or the family physician or community pharmacist may have noticed and corrected the discrepancy in the community setting. In one previous study, 70% of patients had at least one unintentional discrepancy, 30% of which had the potential to cause possible or probable patient discomfort or clinical deterioration.⁴ In another study, 60% of patients had at least one unintended discrepancy, of which 18% were clinically important.⁹ It is possible that the increase in medication discharge discrepancies observed in this study led to an increase in the rate of adverse events experienced by patients, but the impact and significance of the medication discharge discrepancies would require further investigation. Future research correlating medication discrepancies and their clinical consequences is needed but was beyond the scope of the study reported here.

This study utilized the PPI drug class to measure the change in discharge discrepancy rates when there was misalignment between drug products specified in hospital and provincial formularies. It is reasonable to expect similar increases in discrepancy rates with other drug classes for which hospitals have implemented therapeutic interchange protocols, such as angiotensin-converting enzyme inhibitors, angiotensin II

receptor blockers, 3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitors (statins), calcium channel blockers, and H₂ receptor antagonists. Given that all of these drugs are commonly prescribed, the effect of therapeutic interchange and subsequent discharge discrepancies on patient safety can be expected to be broad and substantial.

Savings on the cost of drugs is one of the main reasons for use of therapeutic interchange in hospitals, and there were significant cost differences between formulary and nonformulary PPIs. For example, during the time of this study, costs were \$0.36/day for rabeprazole 20 mg once daily but only \$0.01/day for lansoprazole 30 mg or esomeprazole 40 mg once daily, according to the hospital's contractual pricing for drugs. Thus, there was strong economic motivation to designate lansoprazole and esomeprazole in the hospital's formulary. However, the results of this study indicate that the economic benefits of misalignment between hospital and PharmaCare formularies for PPIs come at the cost of a significant increase in discharge discrepancies.

CONCLUSIONS

Misalignment between the PPI designated in the study hospital's formulary and the PPI designated in the BC PharmaCare formulary was associated with a significant increase in the rate of discharge discrepancies, related to use of a hospital therapeutic interchange protocol.

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