

Appropriateness of omeprazole prescribing in Quebec's senior population

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BACKGROUND: Prescribing omeprazole for the treatment of digestive disorders accounts for an important part of the costs in Quebec's drug benefit plan. In July 1993, the Quebec drug program listed omeprazole, with restriction, in its formulary. On January 1, 1994, this restriction was lifted; since then, omeprazole has been listed in the regular provincial formulary.

OBJECTIVE: To describe the appropriateness of initial omeprazole prescribing in the ambulatory senior population of Quebec in the 27 months after being listed without restriction.

SUBJECTS AND METHODS: A retrospective population-based cohort study was performed using prescription and medical services claims databases of the Quebec drug program. Data were extracted for elderly patients who received their first omeprazole prescription between July 1, 1994 and March 31, 1996.

RESULTS: Among the 47,140 first-time users of omeprazole identified, 7516 (15.9%) had had an endoscopy in the previous six months, 2308 (4.9%) were given an antimicrobial agent and omeprazole simultaneously, and 22,730 (48.2%) received omeprazole after prior use of an H₂ receptor antagonist (H₂RA) or a prokinetic drug. A total of 26,525 (56.3%) first-time users were prescribed omeprazole based on at least one of the three criteria listed above. Among these users, 729 (2.8%) received an H₂RA concurrently with omeprazole. Altogether, 25,796 (54.7%) first-time users received omeprazole appropriately.

CONCLUSIONS: Although reimbursement for omeprazole prescriptions has not been restricted in Quebec since January 1, 1994, it was prescribed appropriately for elderly patients in the majority of cases studied.

Key Words: Administrative database; Appropriateness of prescribing; Drug use review; Elderly patients; Omeprazole

Pertinence des prescriptions d'oméprazole chez les personnes âgées au Québec

CONTEXTE : Les prescriptions d'oméprazole pour le traitement de troubles digestifs constituent une part importante des coûts du régime d'assurance-médicaments au Québec. En juillet 1993, l'oméprazole était inscrit sur la liste du programme de médicaments du Québec, mais avec certaines restrictions. Ces restrictions ont été levées le 1^{er} janvier 1994. Depuis, l'oméprazole figure sur la liste provinciale des médicaments admissibles.

OBJECTIF : Examiner la pertinence des prescriptions d'oméprazole comme traitement initial chez les patients âgés ambulatoires au Québec, et ce, 27 mois après la levée des restrictions.

POPULATION ET MÉTHODE : Une étude rétrospective de cohortes, fondée sur la population a été menée à partir des bases de données du programme de médicaments du Québec pour les demandes de règlement des prescriptions et des services médicaux. Les données recueillies concernaient les patients âgés qui avaient obtenu leur première prescription d'oméprazole entre le 1^{er} juillet 1994 et le 31 mars 1996.

RÉSULTATS : Parmi les 47 140 patients ayant obtenu une première prescription d'oméprazole, 7 516 (15,9 %) avaient subi une endoscopie au cours des six mois précédents, 2 308 (4,9 %) étaient soumis à une bithérapie composée d'un agent antimicrobien et de l'oméprazole et 22 730 (48,2 %) prenaient de l'oméprazole après avoir utilisé un inhibiteur des récepteurs H₂ ou un agent pro-cinétique. Au total, 26 525 patients (56,3 %) se sont vu prescrire de l'oméprazole pour la première fois suivant l'un des trois critères précités. Parmi ces patients, 729 (2,8 %) prenaient de l'oméprazole en association avec un inhibiteur des récepteurs H₂. Dans l'ensemble, la première prescription d'oméprazole s'est avérée pertinente chez 25 796 patients (54,7 %).

CONCLUSION : Même si le remboursement du coût de l'oméprazole ne fait pas l'objet de restriction depuis le 1^{er} janvier 1994, les prescriptions d'oméprazole chez les personnes âgées se sont révélées appropriées dans la majorité des cas étudiés.

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In Canada's public drug benefit plans, a substantial portion of drug expenditure is attributed to the prescription of gastrointestinal drugs. In Quebec's drug program, gastrointestinal drugs given to elderly patients accounted for 8.5% of drug costs in 1994, 9.0% in 1995 and 9.4% in 1996 (1). During this period, proton pump inhibitors (PPIs) were among the most frequently prescribed classes of gastrointestinal drugs in Quebec.

The first PPI, omeprazole, was approved for the Canadian prescription drug market in 1989. In 1996, omeprazole was the medication with the greatest market share in Canada, with sales of over CDN\$182 million (2).

PPIs are effective in the treatment of many gastrointestinal disorders including peptic ulcers, gastroesophageal reflux disease, Zollinger-Ellison syndrome and *Helicobacter pylori* infection (3-6). PPIs should be used as first-line agents in the treatment of Zollinger-Ellison syndrome (4,7-10) and moderate to severe reflux esophagitis that is confirmed by endoscopy (11-21). To eradicate *H. pylori*, the use of PPIs in combination with one or more of the following antibiotics for either seven (22-24) or 14 (25,26) days of therapy has been suggested: amoxicillin, clarithromycin, metronidazole and tetracycline.

Like H_2 receptor antagonists (H2RAs), PPIs are a therapeutic option in the treatment of peptic ulcers. However, because an advantage of PPIs over H2RAs is observed mainly in patients with refractory peptic ulcers (4,27-30), studies published before 1996 recommended the restricted use of PPIs as second-line agents in gastric and duodenal ulcers (30-32). Prescribing a prokinetic drug or an H2RA first and restricting PPI use to resistant cases have been recommended for the treatment of uncomplicated gastroesophageal reflux disease (3,17,20,32-34).

Concerned about costs, several provincial drug benefit plans in Canada have listed PPIs with restriction on their formulary. In general, the utilization criteria of these plans allow PPIs to be prescribed as second-line agents only (35). In Quebec, omeprazole was on the restricted formulary from July to December 1993. During this period, before reimbursement could be authorized, omeprazole prescription for elderly patients in an ambulatory setting required a written justification sent by the prescriber to the public drug plan. Payment was made upon acknowledgement of the indication. On January 1, 1994, this restriction was lifted and omeprazole was listed on the regular provincial formulary. After this time, we thought that omeprazole might have been inappropriately prescribed for Quebec's elderly patients.

The objective of the present study was to describe the appropriateness of initial omeprazole prescribing during the 27 months after being listed without restriction for treatment of the ambulatory senior population of Quebec.

SUBJECTS AND METHODS

A retrospective, population-based cohort study was performed with the use of two databases administered by the Régie de l'Assurance Maladie du Québec (RAMQ) – the prescription and pharmacy services claims database and the

medical services claims database. These databases provide information on pharmaceutical and medical services received by Quebec's noninstitutionalized seniors (aged 65 years or over) and welfare recipients. All Quebec seniors who received their first prescription for omeprazole between July 1, 1994 and March 31, 1996 were included in the study population. These first-time users had not filled a prescription for omeprazole in the previous six months.

For each first-time user, prior treatments with an H2RA or a prokinetic drug, and concurrent prescriptions for H2RA were assessed. The H2RA drugs considered were cimetidine, famotidine, nizatidine and ranitidine. The prokinetic drugs considered were cisapride, domperidone and metoclopramide.

Appropriateness of omeprazole prescribing was assessed by using criteria developed after a review of the scientific literature published before 1996. According to these criteria, a first prescription for omeprazole was considered appropriate if the user had had an upper gastrointestinal endoscopy in the previous six months; if the omeprazole was dispensed at the same time as a seven- to 14-day course of antimicrobial therapy with amoxicillin, clarithromycin, metronidazole or tetracycline; or if the omeprazole prescription had been preceded by an H2RA or a prokinetic drug prescription within the previous six months.

However, when an H2RA was used concurrently with omeprazole, the prescription was automatically considered inappropriate. Concurrent use of H2RA was defined as delivery of H2RA within the duration of the first omeprazole prescription. To ensure that prescribing an H2RA was not a change of treatment, a second omeprazole prescription had to be given during the course of the H2RA prescription.

To preserve user anonymity, data transmitted by RAMQ were encoded. Data from prescription claims and medical services claims databases were matched by using patients' individual identifying numbers. Prescriptions and medical services billed between January 1, 1994 and June 30, 1996 were analyzed.

The proportion of Quebec's senior population who received a first omeprazole prescription during the study period was calculated. The proportion of first-time users receiving omeprazole appropriately was also calculated. Variation in the appropriateness of omeprazole prescribing was determined according to prescriber specialty. A χ^2 test with an a priori level of 0.05 was used to compare the proportions of appropriate prescribing among prescriber specialties. All analyses were performed using the SAS statistical software package version 6.12 (SAS Institute Inc, USA).

RESULTS

Between July 1, 1994 and March 31, 1996, 47,140 Quebec seniors received their first prescription for omeprazole; 5.5% of them were identified as first-time users of omeprazole based on the assumption that the number of seniors eligible for the provincial drug plan in 1995 (n=854,280) remained constant during this time period.

Among first-time users of omeprazole, 7516 (15.9%) had

TABLE 1
Appropriateness of prescribing omeprazole to 47,140
first-time users according to the criteria applied

Criteria	Number of first-time users of omeprazole (%)
Upper gastrointestinal endoscopy in the prior six months	
Yes	7516 (15.9)
No	39,624 (84.1)
Number of antibiotics* used concurrently	
Zero	44,832 (95.1)
One	1537 (3.3)
Two	771 (1.6)
Prior use of an H2RA [†]	
Yes	20,205 (42.9)
No	26,935 (57.1)
Prior use of a prokinetic drug [‡]	
Yes	6535 (13.9)
No	40,605 (86.1)
Concurrent use of an H2RA [†]	
Yes	801 (1.7)
No	46,339 (98.3)

*Amoxicillin, clarithromycin, metronidazole or tetracycline; [†]Cimetidine, famotidine, nizatidine or ranitidine; [‡]Cisapride, domperidone or metoclopramide

had an endoscopy in the six months before receiving their first prescription (Table 1). A total of 2308 (4.9%) seniors were prescribed at least one antimicrobial agent and omeprazole at the same time; 771 of these patients (33.4%) received two antibiotics. Combinations of amoxicillin and metronidazole, clarithromycin and metronidazole, and tetracycline and metronidazole were dispensed to 226, 258 and 243 individuals, respectively. The remaining 44 individuals received other combinations of these antibiotics. A total of 22,730 (48.2%) first-time users of omeprazole received this medication after prior use of an H2RA or a prokinetic drug. Overall, 26,525 (56.3%) first-time prescriptions of omeprazole met at least one of the three above criteria of appropriate use. However, 729 (2.8%) of these prescriptions were received concurrently with an H2RA prescription. Consequently, 25,796 (54.7%) first-time omeprazole prescriptions were classified as being appropriate.

General practitioners wrote 70.1% of first-time omeprazole prescriptions. Appropriateness of prescribing was higher among gastroenterologists. In fact, 71.7% of omeprazole prescriptions written by gastroenterologists were appropriate compared with 51.8% ($P<0.01$) of those written by general practitioners and 53.6% ($P<0.01$) of those written by internists.

DISCUSSION

According to our criteria, 54.7% of first omeprazole prescriptions for the senior population of Quebec were appropriate. This proportion is high, especially when compared with results of other studies performed in Canada (36) or elsewhere

(37,38), and more specifically with the findings of two studies performed around the same time period – one in the ambulatory setting in Ontario (35) and one in the hospital setting in Quebec (39).

McBride et al (35) studied the prevalence of appropriate omeprazole prescribing for the ambulatory senior population of Ontario from April 1992 to March 1993. They determined that only 20% of Ontario seniors received omeprazole appropriately. When their study took place, omeprazole was in the restricted formulary in Ontario. Thus, an omeprazole prescription for a recipient of the Ontario Drug Benefit program required written justification of the indication by the prescriber, plus acknowledgement of this indication by the pharmacist, before being filled. The Ontario Drug Benefit criteria permitted the prescription of omeprazole after a trial of at least four weeks of an H2RA. Concurring with Ontario's criteria, McBride et al (35) considered a first omeprazole prescription to be appropriate if it was not preceded by an H2RA prescription within one to six months.

In our study, we considered omeprazole prescriptions that occurred less than one month after receipt of a prescription for an H2RA to be appropriate. We used a less stringent criterion because a shorter therapeutic trial may be justified by side effects (36), drug interactions (40) or other relevant clinical factors. Even so, had we defined appropriate prescribing by using the same criterion as that of McBride et al (35), 37.6% of omeprazole prescriptions for Quebec's seniors would still have been classified as appropriate. Thus, the prescription of omeprazole appears to be more appropriate for Quebec seniors than for Ontario seniors, even without a limited-use program in Quebec. This unexpected difference in the appropriateness of omeprazole prescribing between the two provincial jurisdictions may indicate that restrictive policies do not always succeed in promoting the appropriate use of a drug and that many factors determine the quality of prescribing.

In 1993, the Réseau de revue d'utilisation des médicaments (RRUM) conducted a retrospective review of omeprazole use in 13 hospitals (39). At the time of this review, omeprazole was in the restricted formulary of the provincial drug plan. Altogether, 24% of the acute treatments with omeprazole were initiated outside the hospital. Results showed that only 45% of in-hospital prescriptions for omeprazole were appropriate with regard to indications for acute therapy. According to these criteria, use of omeprazole was appropriate for the treatment of duodenal ulcers refractory to H2RA, gastric ulcers confirmed by endoscopy and refractory to H2RA, reflux esophagitis refractory to H2RA or prokinetic drugs, moderate or severe reflux esophagitis confirmed by endoscopy, and Zollinger-Ellison syndrome. The appropriateness of omeprazole prescribing was, therefore, lower in this review of omeprazole use than in the present study. There are many possible explanations for this difference, including variation in population characteristics, variability in physician prescribing habits, discrepancy in length of the studies, and difference in the data collecting methods and indicators of good prescribing practice used.

In our study, prescribing by general practitioners was significantly more questionable than prescribing by gastroenterologists. In 1991, a similar finding was observed by Moride et al (41) in a study aimed at identifying determinants of suboptimal antiulcer medication use among elderly participants of the Quebec drug plan. One of the predictors for unusually short term use of antiulcer medications was prescribing by a general practitioner. Gastroenterologists may be more familiar with consensus guidelines in their discipline than are general practitioners. Gastroenterologists may also be more likely to prescribe omeprazole as a second-line therapy because they are consulted later in the course of the illness. Further studies should focus on the identification of factors explaining why suboptimal prescribing is associated with the prescriber's specialty.

During the study period, some therapies using a combination of omeprazole and an antibiotic were recommended by, among others, the National Institutes of Health Consensus Development Conference on *Helicobacter pylori* (26). We considered the concurrent use of omeprazole and amoxicillin, clarithromycin, metronidazole or tetracycline as an indication for *H pylori* eradication. Because these antimicrobial agents may be used over seven to 14 days of treatment for a wide array of indications, this particular criterion may have overestimated the appropriateness of omeprazole prescribing. Nevertheless, such overestimation is probably very small because only 4.9% of patients received their first omeprazole prescription at the same time that they received an antibiotic prescription.

The literature published before 1996 supported the use of omeprazole as a second-line alternative to an H2RA in the treatment of peptic ulcers, and to an H2RA or a prokinetic drug in the treatment of uncomplicated gastroesophageal reflux disease. However, we were unable to assess indication for use, trial duration and posology of former treatment with an H2RA or a prokinetic drug. Therefore, the criteria used to define appropriate second-line therapy as an H2RA or a

prokinetic drug taken in the previous six months may have led to an overestimation of appropriateness.

According to Tamblyn et al (42), the prescription claims database of the RAMQ may be one of the most accurate sources of information on drugs dispensed to individuals. Nevertheless, there are still some limitations to the use of this administrative database in studying ambulatory drug prescribing; for example, most clinical factors that could justify the selection of a drug are not recorded in it. Consequently, only prescriptions that are potentially inappropriate can be screened in a drug use review such as this. To judge definitively the quality of drug use, further indepth review of deviant cases is required. Such a review would likely reveal a higher level of appropriateness of use (43) than was found in the present study.

Since 1996, indications for the use of omeprazole have changed. For instance, prescribing a double therapy for *H pylori* eradication is no longer supported by the consensus guidelines (44,45); only triple and quadruple eradication regimens are recommended. Further research is needed to evaluate the current quality of omeprazole prescription.

In June 1996, a universal public drug plan was implemented in Quebec; since then, the annual contribution of the elderly to the drug plan has increased. Whether this change in program modalities affected the appropriateness of omeprazole use in Quebec's elderly population is unknown.

The present study suggests that the level of appropriateness of omeprazole prescribing might not be lower in a program where a drug is listed without restriction than in a more controlled environment. In Canada, there is wide variation across provincial drug plans in terms of eligibility, co-payments and conditions for reimbursement of drugs in formularies. To what extent this variation translates to the quality of prescribing warrants further research.

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