

Consumer Usage Patterns of Nonprescription Histamine₂-Receptor Antagonists

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- OBJECTIVE:** Prescription to over-the-counter (OTC) drug switches are increasingly common. Yet little is known about how the public uses these reclassified products. Histamine₂-receptor antagonists (H₂RAs) are popular examples, although they may be supplanted by OTC proton pump inhibitors (PPIs). We examined the extent to which consumers substitute OTC H₂RAs for physician care and/or engage in off-label use of these medications.
- METHODS:** Self-administered anonymous survey of 1,116 adult OTC H₂RA consumers in a random sample of 20 Los Angeles pharmacies from a major retail chain. Off-label use was defined by FDA warning label (e.g., bloody stools, dysphagia). Substitution was defined by intent to use H₂RA instead of going to a physician.
- RESULTS:** Forty-six percent engaged in off-label use of OTC H₂RAs. Off-label use was independently associated with lower income, substitution for physician care, prior gastrointestinal disease, and past prescription H₂RA use. Thirty-four percent substituted OTC H₂RA use for physician care, and 54% of these met the criteria for off-label use. Substitution was associated with lack of health insurance, lack of time to see a physician, the belief that OTC H₂RA was cheaper than clinic visits, and nonwhite race.
- CONCLUSION:** Almost one-half of adult consumers reported using OTC H₂RAs in a manner inconsistent with FDA labeling, and this off-label use was associated with substitution for physician care. Traditionally vulnerable populations were more prone to off-label use and to substituting H₂RAs for physician care. Further studies are needed to assess patient outcomes, identify remedies, and explore implications for the reclassification of PPIs.

INTRODUCTION

The “Rx-to-OTC” switch is a recent trend in which prescription drugs are reclassified to over-the-counter (OTC) status (1). Reclassified medications are popular with consumers who view them as strong, effective therapies (2). In 1993 alone, nine of the top 10 selling OTC drugs were reclassified products (3, 15). Annual sales of OTC drugs are predicted to reach around \$22 billion by 2010 (2). These changes have spawned new patterns of consumer self-care behavior and raised concerns regarding proper usage by the public (4).

These concerns are intensely debated among members of the Food and Drug Administration (FDA), health insurance companies, the pharmaceutical industry, consumer groups, and health-care providers in regard to the reclassification of a top-selling class of prescription drugs, the proton pump inhibitors (PPIs) (5). While proponents believe reclassification

lowers drug prices, decreases health services utilization, and increases consumer access, critics are concerned with improper substitution of self-care for physician care, leading to misuse and adverse outcomes such as delayed detection of GI cancers (6–12). To date, most reclassification decisions have been based primarily on preconversion data and simulation-studies (e.g., open-label trials using volunteers in shopping malls) (13, 14). Little is known about how real-world consumers actually use these drugs.

In order to help address this knowledge gap, we conducted a study in a natural setting to observe how consumers are using a popular class of reclassified medications, Histamine₂-receptor antagonists (H₂RAs) (7, 9–11). H₂RAs may serve as a proxy measure for how consumers will use OTC PPIs. The purpose of our study was to evaluate the extent to which consumers substitute OTC H₂RAs for provider care and/or engage in off-label use of these medications.

METHODS

Overall Design

A cross-sectional survey of OTC H2RA purchasers (N = 1116) in 20 retail pharmacies throughout Los Angeles County over 4 wk in the fall of 2002.

Sampling of Pharmacies and Consumers

The headquarters of a national retail pharmacy chain provided a list of their 74 pharmacies in Los Angeles County. Twenty pharmacies were selected from this list using simple random sampling method to serve as survey sites. Our target population included all OTC H2RA purchasers in each pharmacy during the sampling period.

Data Collection

Data collection began at the pharmacies on different days over 2 wks beginning on September 12, 2002. Each pharmacy was given an equal 4-wk period from their start date for data collection. Customers were recruited by bilingual (English/Spanish) shelf advertisements next to the OTC H2RA products that directed them to the pharmacy counter to complete a questionnaire. Participants were ≥ 18 yr old and purchased an OTC H2RA product (Tagamet, Zantac, Pepcid, or the generic acid reducer) for personal use. Participants received a one-time \$5.00 discount on the purchase price and paid out-of-pocket for the remainder cost. To minimize any study effects on consumer behavior, pharmacists were neither prohibited nor encouraged to recommend H2RAs to the consumers. The consumers were not instructed to read the package labels/inserts while completing the questionnaire, though they may have. The survey response rate was calculated as the number of surveys returned divided by the number of boxes sold during the study period. For reliability assurance, we verified the sales count with manual and computer tracking.

Survey Instrument

Participants completed a self-administered, anonymous, 21-item questionnaire in either English or Spanish. The questionnaire asked about demographics, symptoms prompting use, prior history of GI disease and previous endoscopic procedures, prior use of prescription H2RAs, provider contact (e.g., through telephone, clinic visit, and/or future appointment), other concurrent pharmacologic therapies, medical contraindications to OTC H2RAs, reasons for purchase, and global health status. It required 3–5 min to complete. The Spanish version was professionally forward and backward translated. The questionnaire had a Flescher–Kincaid grade level of 6.3 and Flescher reading ease score of 66. While completing the questionnaires, the pilot participants reported no difficulty with the vocabulary, sentence or text structure, and the concept of each item. Questionnaires in both languages were pretested for readability and comprehension using one-on-one cognitive interviews with 30 clinic patients and 53 actual OTC H2RA customers in four pilot pharmacies. Pilot data were excluded from the analysis.

Outcome Measures

OFF-LABEL USE. The explicit criteria for off-label use was based on FDA package labels, which instructed against use if one has: trouble swallowing, bloody or black stools, unintentional weight loss, pregnancy, concurrent use of warfarin, or use of ≥ 2 H2RA products concurrently (16, 17). Consumers were scored as off-label users if they reported any of the above conditions. In addition, we also evaluated the number of consumers who met the guidelines from the American Gastroenterological Association, which recommends medical evaluation for individuals ≥ 45 yr old with new-onset dyspepsia (18).

SUBSTITUTION. We asked consumers “Are you using this medicine instead of going to see a health-care provider?” An affirmative answer was scored as substitution. Although our study is based on intent to substitute, previous literatures have shown that intent is linked to action and purchase is linked to use (19–21).

Independent Variables

The modified Anderson Behavioral model (22), tested in a similar study (23), was used to conceptualize factors affecting consumers’ decisions to use OTC H2RAs for self-care versus seeking medical care. Among the factors influencing consumers’ decision-making, we included advertising, waiting for a medical appointment, friend/family’s advice, provider’s advice, pharmacist’s advice, lack of time to visit a provider, the belief that OTC H2RA was cheaper than a clinic visit, a personal dislike of providers, package information, and demographic characteristics including insurance status.

Statistical Analysis

Respondent weights were calculated to correct for inter-pharmacy site differences in nonresponse rates. The design effect from weighting and clustering was minimal. Statistical analyses were performed using the Intercooled STATA 7.0 survey commands (College Station, Texas, 2001). For building regression models, missing data other than demographic variables and outcome variables were replaced using simple hotdeck imputation. Of the 1,116 surveys returned, three were excluded because the drug was purchased for pet use and eight because the subjects reported age < 18 yr old, leaving a total of 1,105 for analysis.

We checked for multicollinearity using zero-order correlation matrices and identified potential predictors of inappropriate use and substitution through bivariate Pearson χ^2 -coefficients and independent sample *t*-tests. Twenty variables with a bivariate association of *p*-value ≤ 0.2 were entered into the multiple logistic regression model to predict substitution and 13 variables for off-label use. Five variables with *p*-values ≤ 0.05 were retained in each of the final models. Forward, backward, and stepwise regression demonstrated no change in the direction of variable significance. The goodness of fit model was evaluated by applying the Hosmer–Lemeshow

test on 10 distinct groups. Doing so, we obtained *p*-values of 0.87 and 0.76 for the substitution and off-label use models, respectively (24).

RESULTS

A total of 1,904 boxes were sold and 1,116 consumers completed our questionnaire (929 English and 187 Spanish), yielding a 57% survey response rate. Table 1 shows the char-

Table 1. Overall Population Characteristics

	n	Unweighted (%)
Gender		
Male	541	50
Female	538	50
Ethnicity		
Whites	485	45
Nonwhites	594	55
Education		
Below high school	78	7
Some high school	94	9
High school graduate	234	22
Some college	277	26
College graduate	273	25
Postgraduate	115	11
Annual household income		
<\$30,000	452	44
\$30,001–\$70,000	359	35
>\$70,001	217	21
Health insurance		
No	245	23
Yes	823	77
History of GI disease		
No	650	60
Yes	350	33
Uncertain	77	7
Previous endoscopy		
No	721	67
Yes	328	30
Uncertain	28	3
Previous use of prescription H2RA		
No	539	51
Yes	524	49
Symptoms		
Heartburn/acid indigestion	922	85
Stomach pain	389	35
Nausea	175	16
Repeated vomiting	61	6
Trouble swallowing	62	6
Diarrhea	79	7
Bloody or black stool	29	3
Constipation	118	11
Fever	28	3
Weight loss	36	3
Other	48	4
Concurrent use of medications		
NSAIDs	339	31
OTC antacid/antidiarrheal agents	196	18
Two or more H2-blocker	438	41
Coumadin or blood thinning agents	23	2
Misc medicine for comorbid conditions	136	13

Table 2. Logistic Regression Model—Factors Associated with Improper/Off-label Use of OTC H2RA

Factors	Adjusted OR* (95% C.I.)	<i>p</i> -Value
Substitution for provider care	1.43 (1.06–1.92)	0.001
History of GI disease	1.74 (1.41–2.14)	0.000
Previous use of prescription H2RAs	1.67 (1.34–2.09)	0.000
Concurrent use of OTC antacid/antidiarrheal agents	2.04 (1.42–2.92)	0.000
Annual household income	0.63 (0.49–0.81)	0.001

*Adjusted for the effects of other variables in the model.

acteristics of respondents. We also evaluated whether the \$5.00 incentive induced any spurious sales increase by comparing sales data from before and during the study and found no increase in sales during the study period.¹

Almost half of respondents (46%, *n* = 512) met the FDA package label warning criteria. Specifically, there were 28 self-reports of bloody/black stool, 61 of dysphagia, 35 of weight loss, 8 of pregnancy, 23 of concurrent use of warfarin, and 438 of concomitant use of two or more OTC H2RA products. While some reports originated from the same consumer, most came from different individuals. Excluding concomitant H2RA use, 131 (12%) individuals still reported an off-label use. When asked how much the package information influenced their purchasing decision, 68% of the respondents answered “not at all.” Of the total 512 cases of off-label use, 89 (17%) had never seen or spoken to a health-care provider about their symptoms. Forty-two of these 89 cases lacked health insurance. An additional 65 consumers reported new-onset dyspepsia and were age 45 or older, meeting the American Gastroenterological Association guideline for medical evaluation (18).

One-third of respondents (33%) reported substituting OTC H2RA use for provider care. Of these individuals, 54% met the criteria for off-label use, 37% lacked health insurance coverage, and 29% were Spanish-speaking.

Results of final logistic regression models for off-label use and substitution for physician care are shown in Tables 2 and 3, respectively. Lower annual household income and concurrent use of OTC antacids or antidiarrheal agents remained significant in the off-label use models, even if off-label use was redefined to exclude those cases reporting concurrent use of two or more H2RAs.

DISCUSSION

This current, real-world survey of OTC H2RA consumers in a random sample of Los Angeles pharmacies demonstrated high levels of off-label use and substitution for provider

¹During the 4 wk before the start of our study, 19 out of 20 pharmacies sold a total of 1,917 boxes (due to management, one pharmacy declined to provide prestudy sales data but did provide subsequent sales data during the study period). The same 19 pharmacies sold a total of 1,848 boxes during the 4 wk study period.

Table 3. Logistic Regression Model—Factors Associated with Substitution of OTC H2RA for Physician Care

Factors	Adjusted OR* (95% C.I.)	p-Value
White race	0.54 (0.39–0.74)	0.000
Health insurance	0.35 (0.23–0.54)	0.000
Belief that OTC H2RA is cheaper than provider visit	1.33 (1.19–1.50)	0.000
Lack of time to see provider	1.26 (1.10–1.44)	0.002
Dislike providers	1.16 (1.02–1.32)	0.023

*Adjusted for the effects of other variables in the model.

care. These findings are especially significant because greater odds of off-label use were found among those with a history of GI disease and former use of prescription H2RAs. Off-label use was also associated with concomitant use of OTC antacids/antidiarrheal agents, suggesting potentially harmful polypharmacy and experimentation with OTC medications. Even excluding concomitant use of two or more OTC H2RAs, 12% of consumers still fit the criteria for off-label use. This off-label use was especially common among low-income consumers. Furthermore, off-label use was linked to substitution of OTC H2RAs for provider care. Because substitution was, in turn, associated with barriers to access of care (e.g., lack of health insurance or time to see physician), it may be that an already vulnerable population resorts to these drugs with increased risk of misuse leading to undertreated GI diseases.

This study has several strengths. First, our novel method involved multiple, randomly selected pharmacies located throughout a large metropolitan setting, thereby capturing the full spectrum of OTC H2RA consumers including those who have seen providers and those who were self-medicating. Second, we studied real-world consumers in order to provide direct insights into their characteristics and use behavior. All participants had willingly visited the pharmacy with the intent to purchase OTC H2RAs before they were exposed to the study, and we minimized any observer effects that might affect their behavior. Last, we utilized a large, well-known pharmacy chain that serves the diverse LA population.

This study has some limitations. First, because the study was cross-sectional and anonymous, we do not have follow-up data to assess how consumers have used the medication at home and their associated health outcomes. Risks of breaching confidentiality prohibited us from identifying consumers in the pharmacies and contacting them later for follow-up data. It is conceivable that some may have read the package label after returning home and decided against using the medication, although purchase usually predicts use (21). Future studies should further examine subsequent consumer behavior and disease outcomes. Second, our study relied on consumer self-reports rather than medical records. Self-reports may be inaccurate, though it is these recollections that the consumer themselves relied upon in making their health-care

decisions. Third, our response rate was conservatively calculated by assuming that each box was independently purchased by a different consumer. Pharmacists reported that some consumers purchased more than one box at a time, but were only allowed to complete one survey. Others purchased the product for friends/family members or for persons younger than 18 yr of age and were ineligible for participation. Though we were unable to quantify these effects, they could have biased the response rate downward. Nevertheless, our sample approximates Los Angeles County's demographics (25).

As an initial step toward understanding public use of a reclassified medication, this study has important implications for drugs, such as PPIs, undergoing a similar process. Presently, the FDA reclassification criteria mandate that a drug should treat an easily self-diagnosed condition, have a history of safety and low potential for misuse or abuse, and have a package label with use instructions and warnings easily comprehended by an average consumer (13, 14). H2RAs are safe medications, but our study raises questions about misuse and effectiveness of package information as a diffusion method for self-care knowledge. Though we did not specifically ask consumers whether they read the package labels or inserts so as to minimize cues that may change their behavior, 68% said the label did not influence their purchasing decision at all. Future reclassification research should evaluate more active methods of promoting appropriate consumer self-care decisions and use behavior.

Although reclassification may increase consumer access to medications, our findings also question whether this access ultimately comes with the price of delayed provider care for more serious health conditions. Despite package instructions to consult a physician, substitution of OTC H2RAs for physician care is common among the uninsured. While OTC status may increase the proportion of the uninsured that benefit from H2RA therapy, it may also perpetuate inappropriate self-care in this already vulnerable group. Further studies are needed to identify remedies that will assure proper and safe usage of this and other reclassified medications by the public.

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