Patient Receipt and Understanding of Written Information Provided with Isotretinoin and Estrogen Prescriptions

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BACKGROUND: Medication guides (MG) and mandatory patient package inserts (MPPI) are required with some prescription medications.

OBJECTIVE: We sought to determine how many patients receive, read, and understand these mandated materials.

DESIGN AND PARTICIPANTS: A total of 3,620 patients were identified as filling prescriptions for isotretinoin or selected estrogen products from February 2004 to January 2005. Patients were surveyed to gauge receipt and understanding of the MG for isotretinoin and the MPPI for estrogen.

MEASUREMENTS AND MAIN RESULTS: A total of 500 patients completed the survey, with 186 (93%) of the 200 isotretinoin patients and 258 (86%) of the 300 estrogen patients reporting receipt of the MG/MPPI with their most recent prescription. The majority of respondents reported confidence in their knowledge of their medication (86% for isotretinoin and 75% for estrogen). However, the mean score on 5 questions assessing recognition of medication risks was only slightly better than the score expected from guessing (3.1 vs 2.5, $P<.01$ for both isotretinoin and estrogen).

CONCLUSIONS: Despite receiving the information and reporting confidence in medication knowledge, patients' understanding of major risks with these medications was poor. This finding highlights the need to develop better risk communication strategies to improve the safe and effective use of prescription medications.

KEY WORDS: medication guide; package insert; drug information; patient education.
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For medications such as all estrogens and drugs that pose a serious or significant public health risk, the U.S. Food and Drug Administration (FDA) requires the distribution of written medication information that had been approved by the FDA.[1,2] For estrogen, this information is known as the mandatory patient package insert (MPPI).[3] For drugs with a high public health risk, the information is called a medication guide (MG).[4,5]

No evaluations have been conducted to assess distribution and patient understanding of the MG/MPPI. The purpose of this study was to assess the frequency with which patients receive, read, and understand the MG for isotretinoin and MPPI for selected estrogen products.

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METHODS

Accutane®, Amnesteem®, and Sotret® were the selected brand-named isotretinoin products, and Premarin® and Activella® were the selected estrogen products. The MG/MPPI is included within the drugs' safety-sealed packaging, except in the case of Premarin, for which the MPPI is distributed separately.

Prescription claims data from a pharmacy benefits manager (PBM) were used to identify patients for survey. Beneficiaries from two participating PBM clients who were ≥18 years of age, English speakers, with a prescription for one of the selected drugs between February 2004 and January 2005 were eligible for the study. Prescription claims were identified every 2 weeks. Equal numbers of patients filling a prescription for each brand-named product within each drug group were sought. Available patient information included age, sex, patient relationship to the insured individual, geographic region, date of prescription, and use of mail-order or retail pharmacy. For those patients who participated in the survey, prescription claims for all medications in the previous 6 months were also obtained. Ten days were allowed for contact of all patients from the end of each 2-week interval. This study was approved by the Duke University Health System Institutional Review Board.

Patient Survey

After giving consent, all patients were asked how confident they were in their knowledge of their medication. A description of the MG/MPPI was read to each patient. Those who remembered receiving the MG/MPPI were asked how thoroughly they read it, how helpful it was, and whether they had received this information with previous prescriptions. Then 5 potential adverse effects/risks were read to each patient. For each, the patient was asked whether the adverse effect/risk could be associated with the use of their medication.

Patients who did not recall receiving the MG/MPPI with their most recent prescription were asked if they had received it with any of their previous prescriptions. Those who stated that they had previously received it were asked the same questions listed above. All remaining patients were only asked questions pertaining to the 5 adverse effects/risks.

Design and Analysis

A survey sample size of 300 estrogen and 200 isotretinoin patients was sought.

Characteristics of respondents and nonrespondents were compared using nonparametric tests. Responses were compared between those patients reporting receipt of the MG/MPPI with the most recent prescription and those who did not receive it. Categorical variables were analyzed using chi-square tests, and continuous variables were analyzed using Wilcoxon two-sample tests. Nonparametric tests were used to make comparisons among the overall number of correct responses to the 5 risk questions between brand-named products within each drug group and to the number of correct responses expected from the use of a random guessing strategy.

A propensity score was developed to predict respondents versus nonrespondents within each drug group using the following baseline variables: age, sex, primarily/secondarily insured, time from filling of prescription to survey date, number of previous prescriptions for same drug group, retail versus mail-order, and survey quarter.

Generalized estimating equation models, using the estimated propensity scores as weights, were used to identify characteristics associated with the number of correct responses to the risk questions.[6] Variables, in addition to those listed above, included completeness of reading of MG/MPPI with current prescription, confidence in drug knowledge, helpfulness of MG/MPPI, past receipt of MG/MPPI, and past completeness of reading of MG/MPPI. The relationship of predictor variables to the estimated number of correct responses was summarized using point estimates and 95% confidence intervals. All statistical comparisons were two-sided with P values <.05 considered statistically significant.

RESULTS

A total of 3,620 patients were identified as filling a prescription for one of the selected drugs. From these, 500 completed surveys were obtained (300 from those receiving estrogen and 200 from those receiving isotretinoin). Reasons for nonresponse included the following: no or incorrect telephone number (1,554, 50%); unreachable (948, 30%); patient refused to listen to the consent (505, 16%); patient unable to speak English (52, 2%); patient refused to participate in the survey (5/<1%); and miscellaneous other reasons (56, 2%).

Patients with Isotretinoin Prescriptions

A total of 172 (86%) of the 200 participants stated that they were very confident/confident that they knew everything necessary to safely take their isotretinoin. Of the 200 respondents, 186 (93%) reported receiving the MG with their most recent isotretinoin prescription. Patient characteristics and survey responses are presented in Table 1. There were no differences in the proportion of patients reporting receipt of the MG among the 3 brand-named isotretinoin products (P=.3),

Table 1. Characteristics and Survey Responses of Responders Who Recalled Receipt of Medication information

Characteristic	Estrogen (*N*=258)	Isotretinoin (*N*=186)
Median age (25th, 75th percentile)	56 (53, 62)	31 (22, 41)
Female sex (%)	258 (100)	128 (69)
Relationship to insured		
Self (%)	158 (61)	96 (52)
Spouse (%)	100 (39)	45 (24)
Dependent/others (%)	0 (0)	45 (24)
Median number of days between filling of prescription and survey (25th, 75th)	18 (15, 24)	18 (13, 24)
Mean number of previous prescription fills of same drug class in previous 6 months (SD)	3.99 (2.34)	2.27 (1.92)
New prescription for selected drug group (%)	39 (15)	108 (58)
Number of patients who obtained drug via mail order (%)	36 (14)	0
Number of patients who obtained drug from a chain pharmacy (%)	219 (85)	160 (86)
Survey quarter		
2004 Q1 (%)	112 (44)	36 (19)
2004 Q2 (%)	38 (15)	57 (31)
2004 Q3 (%)	45 (17)	20 (11)
2004 Q4 (%)	63 (24)	64 (34)
2005 Q1 (%)	0 (0)	9 (5)
Geographic region		
West (%)	3 (1)	0
Northeast (%)	195 (76)	153 (82)
Southeast (%)	58 (22)	33 (18)
Midwest (%)	2 (<1)	0
Unknown (%)	0	0
Reported MG/MPPI receipt by brand		
Accutane, %	–	92
Amnesteem, %	–	92
Sotret, %	–	100
Activella, %	91	–
Premarin, %	81	–
Number of patients who read MG/MPPI with most recent prescription		
Completely, cover to cover (%)	72 (28)	77 (41)
Couple of complete sections (%)	30 (12)	30 (16)
One complete section (%)	6 (2)	1 (<1)
Skimmed (%)	52 (20)	28 (15)
Did not read any of the MG/MPPI (%)	96 (37)	49 (26)
Unknown (%)	2 (<1)	1 (<1)
Number of patients who read MG/MPPI with previous prescription	*N*=222	*N*=104
Completely—cover to cover (%)	122 (55)	62 (60)
Couple of complete sections (%)	29 (13)	16 (15)
One complete section (%)	3 (1)	1 (1)
Skimmed (%)	36 (16)	13 (13)
Did not read any of the MG/MPPI (%)	26 (12)	12 (12)
Unknown (%)	6 (3)	0 (0)
Number of patients who reported MG/MPPI as being very helpful/helpful with most recent prescription (%)	115 (45)	129 (69)

MG Medication guide, MPPI medication patient package inserts, SD standard deviation.

Table 2. Reported Knowledge of Potential Adverse Effects

Question	Number of correct responses (%)
Isotretinoin (*N*=186)	
Accutane/Amnesteem/Sotret may cause bleeding	75 (40)
Accutane/Amnesteem/Sotret may cause birth defects*	179 (96)
Accutane/Amnesteem/Sotret may cause heart attacks	102 (55)
Accutane/Amnesteem/Sotret may cause mental problems or suicide*	157 (84)
Accutane/Amnesteem/Sotret may cause abnormal heart rhythms	67 (36)
Estrogen (*N*=258)	
Premarin/Activella may cause infections	201 (78)
Premarin/Activella may increase the risk of cancer of the uterus*	145 (56)
Premarin/Activella may increase the risk of cancer of the brain	195 (76)
Activella should not be used during pregnancy (*N*=136)*	126 (93)
Premarin may increase the risk of having a heart attack (*N*=122)*	50 (41)
Premarin/Activella may cause abnormal heart rhythms	77 (30)

**Risks that were included in medication guide MG or medication patient package insert MPPI. Only the responses from patients who reported receipt of the MG/MPPI with most recent prescription are included.*

and the only statistically significant difference between those who reported receipt of the MG and those who did not was the median number of days between the filling of prescription and survey (18 vs 22 days, $P=.03$).

The number and proportion of patients who correctly answered each of the questions on the potential risks of isotretinoin are presented in Table 2. The mean number of correct responses was 3.1 ± 1.1, which was only slightly better than the anticipated score of 2.5 from pure guessing ($P<.01$). Results from the propensity-weighted score model predicted the score to increase by 0.6 in patients with a self-reported high level of confidence in their knowledge of isotretinoin and by 0.6 in patients who recently read the entire MG. Of the 115 women between the ages of 18–45, 4 (3.5%) did not report teratogenicity as one of the potential risks of isotretinoin; 1 reported receipt of the MG with the most recent prescription and 3 did not.

Patients with Estrogen Prescriptions

A total of 226 (75%) of the 300 participants stated that they were very confident/confident that they knew everything necessary to safely take their estrogen. Of the 300 respondents, 258 (86%) reported receiving the MPPI with their most recent prescription. Significantly fewer patients reported receiving the MPPI with Premarin than with Activella ($P=.02$). There were no differences in any of the collected characteristics between those patients who reported receipt of the MPPI and those who did not (Table 1).

The number and proportion of patients who correctly answered each of the questions on potential risks of estrogen are presented in Table 2. The mean number of correct responses was 3.1 ± 1.1, which was only slightly better than the anticipated score of 2.5 achieved from guessing ($P<.01$). The propensity-weighted score model predicted an increase in score by 0.4 and 0.7 for patients who found the MPPI very helpful and for patients who had previously read the MPPI, respectively.

DISCUSSION

Patient medication information is important, especially for chronic medications that are self-administered. Adverse drug events may be reduced among informed patients who are more actively engaged in their own health care.[7,8] The MG/MPPI are the only forms of patient medication information mandated by the FDA. The high proportion of patients who said that they received the MG/MPPI was encouraging, and the relatively lower proportion of patients who reported receipt of the Premarin MPPI indicates that inclusion of the MG/MPPI within the drug packaging is important for patient receipt.

For written medication information to be effective, it must read and understood. While it is encouraging that 94% of all isotretinoin respondents knew of the teratogenic risk (96% of those who received the MG with most recent prescription), 4 (3.5%) women were at potential risk from their lack of this knowledge. A recent review by the FDA found 120 pregnancies in patients taking isotretinoin in the year after initiation of the System to Manage Accutane-Related Teratogenicity (SMART) risk management program and 127 pregnancies reported in the year before the initiation of the program.[9–11] Our results indicate that, even with a risk management program that includes the MG, some patients were unaware of the potential risk.

For estrogen, knowledge gaps also existed. Fewer than half of the respondents were aware of the myocardial infarction risk despite its emphasis in the MPPI and extensive press coverage, and only slightly more than half were aware of the risk of uterine cancer.[12]

A better process and format for communicating key medication information to patients appears necessary. Potential solutions, such as the development of individualized written information and patient counseling, should be more fully explored.

Study limitations include the unavailability of more complete demographic and medical information, including literacy and socioeconomic status.

Conclusion

The content, presentation, and distribution of medication information should be more rigorously evaluated to identify feasible and cost-effective ways to more successfully educate patients about their medications.

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