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Changes to Prescription Drug Pediatric Labeling: Awareness by Practicing Pediatricians

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Abstract

The US Congress and the US Food and Drug Administration encouraged studies in children so that the labeling information about pediatric use could be updated for pharmaceutical products. Pediatricians receive this updated labeling information through many different sources. A pilot survey was conducted to determine what source pediatricians use to learn about this updated information and whether and when they learned of specific changes. It appears that most pediatricians did not know that there had been recent changes in pediatric drug labels, although changes to drugs that were used more commonly in practice were more likely to be known.

Keywords

pediatric, prescribing information, labeling, pediatrician

Introduction

The US Congress has worked with the US Food and Drug Administration (FDA), the Pharmaceutical Research and Manufacturers Association and other organizations over the past nearly 2 decades to improve information on prescription drugs that is made available to practicing pediatricians. These efforts culminated in both "carrot and stick" stimuli to encourage the pharmaceutical industry to provide appropriate labeling information for children.[1] The FDA Modernization Act of 1997, the Pediatric Research Equity Act of 2007, and the Best Practices for Children Act of 2007 all gave FDA increased abilities to ensure pediatricians have the best information possible to treat their patients.[1]

The question now seems to be whether pediatricians are aware of this newly available information. A Delphi Survey conducted by the National Institutes of Health for the American Academy of Pediatrics in 2005 revealed that the favorite source of labeling information for the majority of the approximately 1000 pediatricians who participated in the survey were sources that were not readily updated.[2] Some of these hardcopy sources may be up to a year out of date when used.

To determine whether pediatricians in clinical practice today are more likely to utilize electronic labeling information, and thus more current information, we designed a pilot survey to ask Michigan pediatricians if they were aware of specific labeling changes made during the previous 2 years.

Methodology

Pediatric labeling changes from April 2010 to December 2011 were gathered from the FDA website. These 25 changes were reviewed by the authors and 2 other pediatricians to generate a list of the 10 drugs thought to the most relevant to practicing pediatricians (Table 1).

An electronic survey was created. The survey asked if the respondent was currently in clinical practice and for how long. For each of the medications, the survey asked (1) if the pediatricians knew of the specific labeling change, (2) whether they used the drug in clinical practice, and (3) when and from what source they learned of the labeling change (if they could recall).

In February 2012 the survey was sent electronically to the email addresses of record of the approximately 1300 members of the Michigan Chapter of the American Academy of

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Table 1. Drugs with labeling changes that were used in the survey.

Brand Name (Generic Name)	Date of Change	Labeling Change
Topamax (topiramate)	Jul 15, 2011	Expanded age range down to 2 years; previously approved for monotherapy for partial onset or primary generalized tonic clonic seizers
Creon (pancrelipase) delayed-release capsule	Jun 10, 2011	New dosage strength of 3000 lipase units to allow for dosing in infants < 12 months of age
Nexium I.V. (esomeprazole sodium)	Apr 29, 2011	Extended indication to pediatrics from one month to 17 years; effectiveness has not been established in infants younger than 1 year of age
Lamictal (lamotrigine) extended-release tablet	Apr 25, 2011	Approved for conversion to monotherapy inpatients > 13 years of age with partial seizures receiving treatment with single epileptic drug
Intuniv (guanfacine)	Feb 25, 2011	Approved for use as an adjuvant therapy for treatment of attention-deficit/ hyperactivity disorder with stimulants in pediatric patients 7 years and older
Nasonex (mometasone)	Jan 19, 2011	Safety and effectiveness for treatment of polyps in children < 18 years of age has not been established
Uroxatral (alfuzosin)	Dec 15, 2010	Uroxatral is not indicated for use in pediatric patients 2-16 years of age
Protopam (pralidoxime)	Sep 8, 2010	Expanded from adults to pediatrics for treatment of poisoning due to organo-phosphates
Zyrtec Allergy (cetirizine)	Sep 3, 2010	Approved for use in 6 years and older; new dosage form
Advil Congestion Relief (ibuprofen/phenylepherine HCl)	May 27, 2010	Indicated for use in 12 years of age and older; not recommended for use in patients < 12 years

Pediatrics. To preserve the anonymity of the study, no identifying information was collected from those who participated. The survey was closed after 2 weeks.

Results

Completed surveys were received from 52 respondents, giving a response rate of 4%, which is typical for this population (D.A.C.F., personal communication, 17 February, 2012).

Of the 52 respondents, all were currently in clinical practice and 77% had been in practice for > 10 years. Data were obtained for 516 (99.2%) of the 520 drugs (10 drugs per survey respondent) possible. Familiarity with the labeling change was further examined by cross-tabulating these results with the use of the product in the pediatrician's clinical practice. Table 2 presents these data for each of the 10 drugs. The table also includes the therapeutic area for each of the 10 surveyed drugs and the time in months from the labeling change to the survey. Table 3 summarizes the total mentions for each source of labeling information that was recalled by the respondents.

Discussion

This survey was conducted to determine whether and how pediatricians were learning of changes to the labeling of prescription drug products used in pediatric clinical practice. While the results are not definitive, it is hoped these data will generate interest for conducting a larger study on this issue.

The results give us some insight into whether knowledge of the labeling change correlates with clinical use, therapeutic class, or time since labeling change. As seen in Table 2, respondents who used the drug in clinical practice were approximately twice as likely to have known of the change as respondents who rarely or did not use the drug in practice (49% vs 23% and 30%, respectively). While the numbers are too small to be statistically tested, the trend fits the hypothesis that clinicians are more likely to be familiar with labeling changes for drugs with which they are most familiar. It is unsettling, however, that even for these more commonly used drugs, awareness that a recent labeling change occurred is likely no better than 50%. Time from label change to the time of the survey varied from 7 months to 21 months (Table 2), certainly sufficient time for this information to have been communicated.

Two possible interpretations exist for the observation that many pediatricians were unaware of label changes for these medications. One explanation is that pediatricians are unaware of these changes and continue to prescribe using outdated information. While this is possible, it would appear from our results that this group is a minority one, as the majority of the respondents who identified a source of label information listed more updated sources for their information. A more likely explanation is that many pediatricians use continuously updated electronic resources and do not realize that the information they're using is the result of an updated label indication. If, however, the information was indeed new to the majority of the respondents, then one must consider a better way to assure prescribers of recent labeling changes.

Table 2. Familiarity with labeling change cross-tabulated by respondent's use of product.

	Topamax (topiramate)	Creon (pancrelipase)	Nexium I.V. (esomeprazole sodium)	Lamictal (lamotrigine)	Intuniv (guanfacine)	Nasonex (mometasone)	Uroxatral (alfuzosin)	Protopam (pralidoxime)	Zyrtec (cetirizine)	Advil CR (ibuprofen/ phenylepherine HCl)	Percentage of Responses Across All Drugs
Total respondents, n	52	52	51	50	52	52	52	51	52	52	—
Respondents who knew of the change, n (%)	11 (21.2)	2 (3.8)	11 (21.2)	8 (15.4)	32 (61.5)	9 (17.3)	2 (3.8)	4 (7.7)	25 (48.1)	14 (26.9)	23.1
Respondents who use drug who knew of this change, n (%)	1 (9.1)	0 (0.0)	4 (36.4)	2 (25.0)	18 (56.3)	8 (88.9)	1 (50.0)	0 (0.0)	23 (92.0)	1 (7.1)	49.2
Respondents who rarely use this drug knew of this change, n (%)	5 (45.5)	1 (50.0)	2 (18.2)	4 (50.0)	12 (37.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)	2 (14.2)	22.9
Respondents who do not use this drug who knew of change, n (%)	5 (45.5)	1 (50.0)	5 (45.5)	2 (25.0)	2 (6.2)	1 (11.1)	1 (50.0)	4 (100.0)	1 (4.0)	11 (78.5)	29.6
Months from label change to Feb 2012 (time of survey)	7	8	10	10	12	13	14	17	17	21	—
Therapeutic area for drug	CNS	GI	GI	CNS	CV	Resp	Repro (effect on detrusor muscle)	GI	Resp	Resp	—

CNS, central nervous system; CV, cardiovascular; GI, gastrointestinal; Resp, respiratory tract; Repro, reproduction, Advil CR, Advil Congestion Relief.

Table 3. Reported source from which respondents came to know of labeling change.

Source of Labeling Change Information	Number of Mentions	Percentage of Total Mentions
Direct mail or email from FDA or manufacturer	20	27
American Academy of Pediatrics website	18	24
Local or in-house source	13	18
Epocrates database	11	15
Harriet Lane Handbook	2	3
Other	10	14
Total mentions	74	—

[a]Does not include those who chose "did not recall."

Table 4. Knowledge of labeling change collapsed by therapeutic class of product.

	CNS (n = 102)	CV (n = 52)	GI (n = 154)	Resp (n = 156)	Repro (n = 52)
Total respondents, n	102	52	154	156	52
Respondents who knew of the change, n (%)	19 (19)	32 (62)	17 (11)	48 (31)	2 (4)
Respondents who use drug who knew of this change, n (%)	3 (16)	18 (56)	4 (24)	32 (67)	1 (50)
Respondents who rarely use this drug who knew of this change, n (%)	9 (47)	12 (38)	3 (18)	3 (6)	0 (0)
Respondents who do not use this drug who knew of change, n (%)	7 (37)	2 (6)	10 (59)	13 (27)	1 (50)

CNS, central nervous system; CV, cardiovascular; GI, gastrointestinal; Resp, respiratory tract; Repro, reproduction.

The results offer no trend of any correlation between knowledge of change and time during the time period tested in this survey. When the data for the 10 drugs tested were collapsed by therapeutic area, the results did not vary appreciably by therapeutic area (Table 4). Perhaps a larger database might indicate that pediatricians might be more likely to keep up to date with the labeling for riskier products, although our limited data do not indicate such a trend.

Finally, no clear trend was seen with how these pediatricians obtain their labeling information (Table 3). The source of information is diverse, and unfortunately some of these sources do not provide "real-time" labeling updates. Compared to 2005 American Academy of Pediatrics survey,[2] our results offer a different profile of source of drug information. Few of our respondents mention Harriet Lane or Physicians' Desk Reference, while these were the 2 most mentioned sources in the American Academy of Pediatrics survey, suggesting a shift away from print resources to electronic ones. Our respondents most mentioned direct mail or email from the manufacturer or FDA. This source is likely the timeliest source of update, and while this is encouraging, it still was mentioned only 27%, out of the total who recalled the source of their learning of the change. Any conclusion would be premature, however, as 44 of the 118 (37%) who knew of the labeling change "did not recall" the source of their knowledge of the labeling change. Further studies are necessary to more accurately determine the source of pediatricians' knowledge of labeling changes.

The results of this pilot study suggest opportunities for future studies. The authors understand the limitations of a small study, but our data indicate that larger studies might help understand whether the efforts that have gone into pediatric pharmaceutical research are being fully utilized by today's practitioners. We suggest a survey that includes pediatricians, family practice physicians, and pediatric nurse practitioners. The sources of labeling information used by these groups as well as the time for each of these sources to publish the new information also need to be explored. Changes in labeling relating to safety, dosing, or efficacy should all be examined. We also suggest an educational campaign by the professional organizations of these 3 professional groups in which the benefits of "real-time" labeling information are emphasized. Ideally, a follow-up survey after these programs would determine if behavior had been influenced and more recent information utilized.

Conclusion

A survey of members of the Michigan Chapter of the American Academy of Pediatrics revealed that fewer than half of the respondents who used specific drugs in their clinical practice knew that their labels had been changed in the previous 2 years. There were no trends related to time since label change or therapeutic class of the drug. Sources of labeling change information were diverse, with most respondents not recalling how they learned of changes.

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Declaration of Conflicting Interests

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