ORIGINAL RESEARCH

Teratogen Use in Women of Childbearing Potential: An Intervention Study

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Purpose: **The purpose of this study was to quantify the number of women of childbearing potential who are prescribed angiotensin-converting enzyme inhibitor (ACE inhibitor), angiotensin receptor blocker (ARB), or HMG-coenzyme A reductase inhibitor (statin) and to determine the number of documented teratogenic risk discussions (risk documentation) before and after educational interventions.**

Methods: **The institutional review board–approved retrospective chart review included female patients ages 15 to 45 years who were prescribed an ACE inhibitor, ARB, or statin between January 1, 2007, and March 1, 2009. Exclusion criteria were tubal ligation and hysterectomy. A survey determined physician knowledge of teratogenic risks and prescribing practices for targeted medications. Educational interventions were implemented. Data was reviewed and analyzed quarterly for 1 year.**

Results: **Baseline analysis included 200 patients. A total of 129 (64.5%) patients were prescribed an ACE inhibitor, 29 (14.5%) were prescribed an ARB, and 88 (44.0%) were prescribed a statin. Risk documentation occurred for 40 (20%) patients. Analysis after intervention of 131 patients revealed that risk documentation was 2.4 times greater than before intervention (odds ratio, 2.4; 95% CI, 1.5–3.9). No significant difference identified in survey responses before and after intervention; however, resident physicians overestimated risk documentation.**

Conclusions: **Physicians' baseline awareness of ACE inhibitor, ARB, or statin teratogenic risks and risk documentation was lacking. Improvement in risk documentation was seen after intervention; however, continual improvement is essential. (J Am Board Fam Med 2011;24:262–271.)**

Keywords: **Angiotensin-converting Enzyme Inhibitor, Angiotensin Receptor Blocker, HMG-CoA Reductase Inhibitor, Pregnancy, Teratogens**

The prevalence of obesity, hypertension (HTN), diabetes mellitus (DM) and hyperlipidemia (HLD) has steadily increased among the United States population as a whole, including among young women. According to the most recent data from the American Heart Association, in 2006, 32.6% of women ≥20 years of age had HTN; 32% had low-density lipoprotein cholesterol greater than 130 mg/dL; 7.9% had physician-diagnosed DM; and 22.2% had prediabetes.[1] Angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) are commonly used to treat HTN and to prevent the progression of renal disease in DM. These medication classes are considered the standard of care in patients with concomitant HTN and DM.[2] Statins (3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors) are the most common medication used to treat HLD and are considered the standard of care in patients with DM and elevated low-density lipoprotein cholesterol.[2]

Use of ACE inhibitors or ARBs during the second and third trimesters of pregnancy presents well-established risks to the developing fetus. Studies in the early 1990s showed a significantly increased risk of oligohydramnios, fetal renal dyspla-

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sia, intrauterine growth restriction, hypocalvaria, anuria, and fetal death.[3] The exact mechanism of these complications remains unknown; however, it is thought that these complications may result from hypoperfusion of the developing fetal kidney.[4] In 1992, the Food and Drug Administration (FDA) issued a black box warning regarding the use of ACE inhibitors and ARBs during the second and third trimesters of pregnancy.[5] An influential study by Cooper and colleagues[6] provided evidence linking use of ACE inhibitors and ARBs during the first trimester to significantly increased risk of fetal malformations of the cardiovascular system and central nervous system. This retrospective chart review of patients enrolled in Tennessee Medicaid identified 209 infants exposed to ACE inhibitors during the first trimester only. Exposed infants had a 3.7-times increased risk of cardiovascular malformations and a 4.3-times increased risk of central nervous system malformations compared with infants with no exposure.[5] Angiotensin II receptors are widely expressed in fetal tissues and may play a role in fetal development; therefore, exposure to ACE inhibitors or ARBs during the first trimester may increase risk of congenital malformation.[5] The FDA subsequently issued a public health advisory cautioning against the use of ACE inhibitors and ARBs in women of reproductive age.[7] These drug classes are currently labeled pregnancy category C (see Table 1) during the first trimester and category D during the second and third trimesters.[8]

Statin use during pregnancy is contraindicated, although there is limited evidence from human studies regarding fetal risk.[9] Numerous human case reports have shown associated congenital anomalies with statin exposure, including vertebral, anal, cardiac, tracheal, esophageal, renal, and limb anomalies.[9] Exposure during the first trimester has also been linked causally with intrauterine fetal growth restriction and fetal demise. Based on the potential for fetal risk and relatively low acute maternal health benefit, statins are labeled pregnancy category X (see Table 1) during all trimesters.[8]

Related to increasing rates of DM, HTN and HLD among the US population, there is increasing potential for inadvertent fetal exposure to ACE inhibitors, ARBs, and statins. Few published studies have addressed physician knowledge and awareness of teratogenic risk when prescribing ACE inhibitors, ARBs, or statins to women of childbearing age. A review of the current literature identified only one study specifically related to this topic. This retrospective cohort study identified women 16 to 45 years of age who were referred to a tertiary HTN clinic in the United Kingdom between January 2004 and October 2006.[4] A total of 101 women met inclusion criteria and 47 (46.5%) were treated with an ACE inhibitor, ARB, or both. Of the women identified who had increased fertility (age $\leq$40 years), 8 were using no contraception and 3 were using barrier contraception methods only. The authors of this study concluded that many general practitioners in the United Kingdom continued to prescribe ACE inhibitors or ARBs to women of childbearing age without adequate regard to the potential for inadvertent fetal harm.[4]

Table 1. Food and Drug Administration (FDA) Pregnancy Category Definitions[8]

FDA Pregnancy Category	Definition
A	Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of a risk in later trimesters), and the possibility of fetal harm seems to be remote.
B	Either animal reproductive studies have not demonstrated a fetal risk but there are no controlled studies of pregnant women, or animal reproductive studies have shown adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of a risk during later trimesters).
C	Either studies in animals have revealed adverse effects on the fetus (teratogenic or embrocidal or other) and there are no controlled studies in women, or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.
D	There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (eg, if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).
X	Studies in animals or human beings have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

Based on current data regarding the potential for serious adverse fetal effects from ACE inhibitor, ARB, or statin use during pregnancy and the paucity of research about physician awareness of these risks, more investigation is needed. The purpose of this study was to quantify the number of women of childbearing age who were prescribed an ACE inhibitors, ARB, or statin and to determine the number of documented teratogenic risk discussions before and after educational interventions.

Methods

This study took place at the St. Vincent Joshua Max Simon Primary Care Center (PCC) in Indianapolis, Indiana, where multidisciplinary health care professionals provide outpatient care, averaging 70,000 patient visits per year. The PCC is a medical residency training facility that consists of several medical disciplines, including family medicine, internal medicine, obstetrics/gynecology, pediatrics, and various specialty clinics. Patient demographics are diverse and include uninsured, Medicare, Medicaid, and privately insured individuals; English- and non-English-speaking individuals; and literate and illiterate individuals.

The study, consisting of a retrospective chart review and a survey to evaluate physician knowledge before and after educational intervention, was reviewed and approved by the St. Vincent Institutional Review Board. The primary outcomes were to quantify the number of women of childbearing age who were prescribed an ACE inhibitor, ARB, or statin and to determine the number of documented teratogenic risk discussions (risk documentation) before and after interventions aimed at prescribing physicians. Secondary outcomes were to determine physician knowledge regarding the teratogenic risks before and after education, to improve physician risk documentation, and to determine physician or patient characteristics affecting risk documentation when prescribing ACE inhibitors, ARBs, or statins.

Female patients 15 to 45 years of age who were prescribed ACE inhibitors, ARBs, and/or statins at a PCC physician clinic visit between January 1, 2007, and March 1, 2009, were identified through computer-generated queries of the electronic medical record (EMR; Allscripts Electronic Health Record, version 10; Chicago, IL). The terms used to identify the patient population included patient appointment and billing encounter, sex, age, and active medication, including brand name or generic, within the targeted class of ACE inhibitor, ARB, or statin. Exclusion criteria were male sex, women not of childbearing age (ie, younger than 15 or older than 45 years of age), and female patients with a documented history of hysterectomy or tubal ligation. Baseline EMR data collected included patient age; targeted medication(s); prescribed contraceptive agent (type/dosage form); documented targeted medication indication (DM, HTN, HLD, other); pregnancy test on prescribing targeted medication; risk documentation with use of targeted medication; postgraduate year (PGY) of resident or faculty physician who prescribed the targeted medication(s); and resident training program.

An anonymous electronic survey was developed in SurveyMonkey to assess only medical residents' baseline knowledge about the appropriate use and risks associated with prescribing targeted medications to women of childbearing age (see Table 2). After the survey, an educational intervention was presented to family medicine, internal medicine, obstetric/gynecology, and transitional medical residents. Faculty physicians were also invited to attend the educational intervention. For physicians who were unable to attend live sessions, the presented slides were available for review via e-mail and an Intranet site. A clinical pharmacist and medical resident presented the 1-hour educational intervention, reviewing common teratogens, current pregnancy categories and limitations, common references for medication use during pregnancy and emphasized the importance of risk documentation when prescribing potentially teratogenic medications. Limitations of the current pregnancy categories presented were based on FDA-proposed changes for pregnancy labeling with the inclusion of 3 principle components: fetal risk summary, clinical considerations, and a data section.[3,10] A survey was administered to the medical residents approximately 1 month after the educational intervention to assess change in physician knowledge and prescribing habits.

After the educational initiative, individual physicians were provided a memo listing their assigned patients of childbearing age who were prescribed ACE inhibitors, ARBs, and/or statins during the baseline study period. Physicians were asked to review the patients along with the indication for targeted medication use and consider alternatives,

Table 2. Survey Administered to Physicians Before and After Educational Initiative

Survey Question	Survey Response	Correct response Before Intervention (n = 36) (n [%])	Correct response After Intervention (n = 38) (n [%])	*P*
1. Which pregnancy drug category are ACE-I and ARB in?	a. A	15 (41.7)	22 (57.9)	.176
	b. B			
	c. C*			
	d. D*			
	e. X			
	f. I don't know			
2. Which pregnancy drug category is statin in?	a. A	10 (27.8)	19 (50)	<.065
	b. B			
	c. C			
	d. D			
	e. X*			
	f. I don't know			
3. ACE-I and ARB primarily affect which fetal system if exposed during the second and third trimester?	a. Lung	23 (63.9)	28 (73.7)	.440
	b. Cardiovascular			
	c. Renal*			
	d. Nervous			
	e. I am unsure			
4. There is increasing evidence that ACE-I/ARB have adverse effects to fetuses exposed during the first trimester.	a. True*	19 (52.8)	33 (86.8)	.650
	b. False			
	c. I am not sure			
5. Statin has been shown to adversely affect fetal development in human studies.	a. True	7 (19.4)	9 (23.7)	.652
	b. False*			
	c. I am not sure			
6. In the past several months have you prescribed an ACE-I, ARB, or statin to any women between the ages of 15 to 45?	a. Yes†	8 (22.2)	10 (26.3)	1.000
	b. No			
	c. I'm not sure			
7. When prescribing ACE-I, ARB, or statin, do you consider the possibility of the patients becoming pregnant while taking the drug?	a. Yes, always†	24 (66.7)	31 (81.6)	.678
	b. Usually†			
	c. Sometimes			
	d. No, never			
8. If you do consider possible pregnancy when prescribing ACE-I/ARB and statin, do you make an effort to document use of contraception and discussion of possible risks?	a. Yes, always†	25 (69.4)	28 (73.7)	.091
	b. Usually†			
	c. Sometimes			
	d. No, never			
	e. I don't consider pregnancy risk when prescribing			
Physician Demographics				
9. Gender	a. Male	19 (52.85)	17 (44.7)	.316
	b. Female	17 (47.2)	21 (55.3)	
10. Current year of residency training	a. PGY-1	16 (44.4)	18 (47.4)	.889
	b. PGY-2	11 (30.6)	10 (26.3)	
	c. PGY-3	8 (22.2)	9 (23.7)	
	d. PGY-4	2 (5.6)	1 (2.6)	

Continued

if appropriate, with lower teratogenic risk. If the targeted medication was continued, the physician was to have a discussion with the patient about the teratogenic risk versus benefit of the medication and document it in the EMR. To facilitate physician risk documentation, an electronic template was developed through a physician-initiated order for medication counseling. The targeted medica-

Table 2. Continued

Survey Question	Survey Response	Correct response Before Intervention (n = 36) (n [%])	Correct response After Intervention (n = 38) (n [%])	*P*
11. Current residency training program	a. FM	13 (36.1)	12 (31.6)	.770
	b. IM	5 (13.9)	8 (21.1)	
	c. FM/IM	5 (13.9)	3 (7.9)	
	d. OB/GYN	9 (25.0)	8 (21.1)	
	e. Transitional	3 (8.3)	7 (18.4)	

*Correct response to survey question.
†Considered preferred answers.
ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; statin, HMG-CoA reductase inhibitors; PGY, postgraduate year; IM, internal medicine; FM, family medicine; OB/GYN, obstetrics/gynecology.

tion—ACE inhibitor, ARB, and/or statin—was selected from a drop-down menu and the following text was inserted into the EMR: "Patient currently prescribed the specified medication and is of childbearing potential. I have discussed with this patient the teratogenic risk associated with this medication, and I have advised the patient on contraceptive measures to prevent pregnancy while taking this medication. The patient has been instructed to stop this medication and contact our office if she is planning to become or suspects that she is pregnant." Physicians were educated on this new process for risk documentation during the educational intervention and it was reinforced through the e-mailed memo as well as one-on-one during clinic.

Data were gathered after the intervention through computer-generated queries to evaluate female patients with a physician clinic visit between September 1, 2009, and December 31, 2009. Inclusion and exclusion criteria and data collected were identical to the initial baseline data. Additional data evaluated during the first quarter included frequency of use of the new electronic template for risk documentation and the number of patients from baseline in whom targeted medication was stopped or risk documentation occurred without a physician clinic visit. Ongoing assessment included quarterly data collection and analysis for a minimum of 1 year.

For this study, risk documentation was considered to be present if a teratogenic risk discussion was documented within the discussion or plan section of the EMR physician note or if the physician used the new electronic template described previously. Data collected before and after the intervention were grouped during analysis as follows: age divided into 2 groups (15 to 40 years of age and 41 to 45 years of age); ACE inhibitors and ARBs combined into one medication category; and patients receiving a combination of targeted medications (ACE inhibitor and statin or ARB and statin). Age was divided into 2 categories, as described above, because women ≤40 years of age have increased fertility and are more likely to become pregnant resulting in inadvertent drug exposure if they are prescribed a targeted medication. ACE inhibitor and ARB medication classes were combined into one medication category because there is no difference in their FDA pregnancy category or teratogenic risk. Lastly, if a patient was prescribed a combination of targeted medications (ACE inhibitor and statin or ARB and statin) and risk documentation only occurred for the ACE inhibitor/ARB medication category, the data were included for analysis. Risk documentation was not excluded for these patients because the physician documented teratogenic risk for at least one of the prescribed combination targeted medications.

Statistical Analysis

Descriptive statistics were conducted for baseline and first-quarter data. Discrete categorical variables and survey results were evaluated by the Fisher's exact test. $P < .05$ was considered significant, and the statistical analyses were conducted using Statistical Package for Social Sciences version 17.0 for Windows (SPSS, Inc., Chicago, IL).

Results

Approximately 15,000 female patients 15 to 45 years of age are currently registered at the PCC. Based on inclusion and exclusion criteria, 200 patients were included in the analysis before interven-

tion and 131 patients were included in the analysis after intervention (see Figure 1). Patients included in the analyses before and after intervention had been prescribed one or more of the targeted medications: ACE inhibitors, ARBs, or statins.

Table 3 displays the demographic data of patients and physicians included in the analyses before and after intervention. There was no significant difference in patient populations with regard to age, medication(s) prescribed, disease state(s), use and method of contraception, and pregnancy test. There was no significant difference in physician demographics based on the type of training program; however, there was a significant difference in the PGY of physician training from before to after intervention ($P < .001$). Overall, these data reveal that a majority of the patients were younger than 40 years of age and were prescribed an ACE inhibitor with HTN indication. In addition, the most frequent prescriber of targeted medications were internal medicine residents both before and after intervention.

Quantifying the number of women of childbearing age who were prescribed a targeted medication(s) and determining the frequency of risk documentation were primary outcomes of this study. There was no difference before or after intervention in the number of women of childbearing age who were prescribed targeted medication(s) (see Table 4). Patients were most frequently prescribed an ACE inhibitor, followed by statin and ARB. Targeted medications prescribed were consistent with disease states treated; HTN was the most common disease state, followed by DM and HLD (see Table 3). Analysis of the presence of risk documentation when targeted medications were prescribed revealed a significant difference after intervention (see Table 4). Before intervention, risk documentation was present in 40 of 200 patients (20%). After intervention, the presence of risk documentation increased to 49 of 131 patients (37.4%). Patients after intervention were 2.4 times more likely to have risk documentation when a targeted medication was prescribed (OR, 2.4; 95% CI, 1.5–3.9).

Further analysis was performed to determine if any patient or physician characteristics affected risk documentation. Both before and after intervention, risk documentation occurred more frequently among patients 15 to 40 years of age (see Figure 2). Before intervention, risk documentation was present in 29.8% of patients 15 to 40 years of age and 3.9% of patients 41 to 45 years of age ($P < .001$). Compared with before intervention, risk documentation increased after intervention among each age group, to 45.2% of patients 15 to 40 years of age and 23.4% of patients 41 to 45 years of age. Risk documentation continued to occur more frequently for patients 15 to 40 years of age ($P = .015$). Risk documentation was also affected by drug class (see Figure 2). Risk documentation occurred more frequently before intervention in patients who were prescribed an ACE inhibitor or ARB. Before intervention, risk documentation was present in 27.7% of patients who were prescribed an ACE inhibitor or ARB, 4.5% of patients who were prescribed a statin, and 15.9% of patients who were prescribed an ACE inhibitor/statin or ARB/statin ($P = .002$). After intervention, risk documentation became more consistent within each drug class for patients who

Figure 1. Patient inclusion and exclusion.

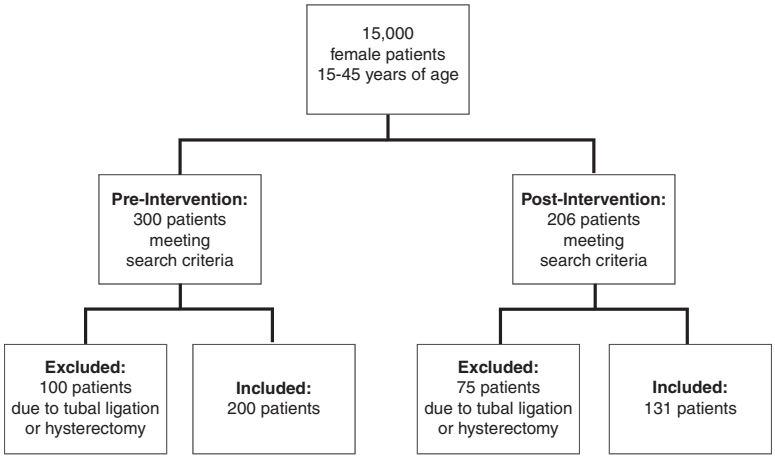


Table 3. Patient and Physician Demographics

Characteristics	Before Intervention (n = 200) (n [%])	After Intervention (n = 131) (n [%])	*P*
Patient			
Age (years)			.728
15 to 40 years old	124 (62.0)	84 (64.1)	
41 to 45 years old	76 (38.0)	47 (35.9)	
Medication prescribed			
ACE-I	129 (64.5)	95 (72.5)	.149
ARB	29 (14.5)	17 (13.0)	.747
Statin	88 (44.0)	50 (38.2)	.307
Disease state indication			
HTN	154 (77.0)	109 (83.2)	.211
DM	88 (44.0)	62 (47.3)	.574
HLD	90 (45.0)	56 (42.7)	.735
Use of contraception*	44 (22.0)	38 (29.0)	.154
Pregnancy test at prescription	5 (2.5)	4 (3.1)	.744
Physician			
Resident training program			.176
IM	102 (51.0)	59 (45.0)	
FM	54 (27.2)	37 (28.2)	
IM/FM combined program	7 (3.5)	9 (6.9)	
OB/GYN	5 (2.5)	0 (0)	
Faculty	32 (16.0)	26 (19.8)	
PGY of Training			<.001
PGY1	0 (0)	15 (11.5)	
PGY2	38 (19)	39 (29.8)	
PGY3	60 (30.0)	43 (32.8)	
Graduate 2009	60 (30.0)	3 (2.3)	
Faculty	35 (17.5)	31 (23.7)	
Graduate	7 (3.5)	0 (0)	

*Method of contraception not different between treatment groups.
ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; statin, HMG-CoA reductase inhibitors; HTN, hypertension; DM, diabetes; HLD, hyperlipidemia; IM, Internal Medicine; FM, Family Medicine; OB/GYN, Obstetrics/Gynecology; PGY, postgraduate year.

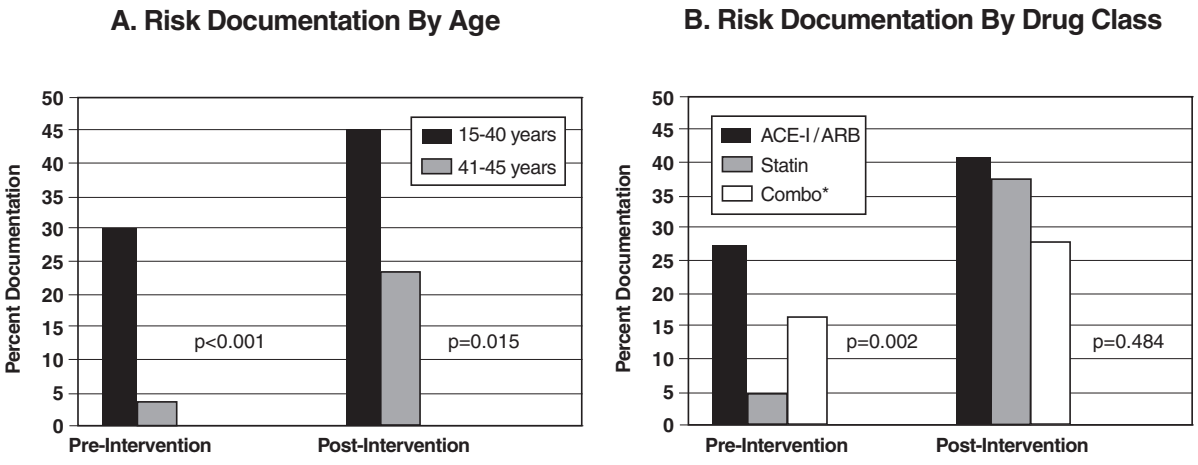
were prescribed targeted medications: 40.7% of patients who were prescribed an ACE inhibitor or ARB, 38.1% of patients who were prescribed a statin, and 27.6% of patients who were prescribed an ACE inhibitor/statin or ARB/statin ($P = .484$). Other patient and physician characteristics that were evaluated but did not significantly affect risk documentation before or after intervention included rate or method of contraception, PGY of resident training or faculty status, and resident training program.

Table 4. Primary Outcome Measures

	Before Intervention (n = 200) (n [%])	After Intervention (n = 131) (n [%])	*P*
Frequency of targeted medications prescribed			
ACE-I	129 (64.5)	95 (72.5)	.149
ARB	29 (14.5)	17 (13.0)	.747
Statin	88 (44.0)	50 (38.2)	.307
Frequency of risk documentation	40 (20)	49 (37.4)	<.001

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; Statin, HMG-CoA reductase inhibitors.

Figure 2. Patient characteristics affecting risk documentation.



*Combo: ACE-I + statin or ARB + statin
ACE-I = Angiotensin-converting enzyme inhibitors; ARB = Angiotensin-receptor blockers; Statin = HMG-CoA reductase inhibitors

Approximately 110 medical residents in internal medicine, family medicine, obstetrics/gynecology, and transitional residency programs were asked to complete the anonymous survey. Thirty-six residents (32.7%) completed the survey before intervention and 38 residents (34.5%) completed the survey after intervention. Table 2 displays the survey results. There was no significant difference in any survey responses or physician demographic data after intervention. Question 6 evaluated how frequently residents remembered prescribing a targeted during the past several months. Before intervention, 22.2% of residents, and after intervention, 26.3% of residents responded that they remembered prescribing targeted medications to women of childbearing age. Questions 7 and 8 addressed the possibility of a woman becoming pregnant while taking targeted medications and risk documentation. Both before and after intervention, approximately 70% of the survey participants considered the potential for pregnancy and responded documenting this risk; however, the retrospective chart review revealed that risk documentation occurred only 20% before and 37.4% after intervention.

In addition to the survey and educational intervention, two other interventions were implemented to increase risk documentation with targeted medications. For patient safety, a memo was sent to physicians with an individualized list of patients who were prescribed targeted medications. Thus, 20 patients who received targeted medications had the medication(s) discontinued independent of an office visit. Creation and implementation of the new electronic template within the EMR was used for 28 of the 49 patients (57.1%) for whom risk documentation occurred after intervention.

Discussion

This study reveals a need to educate physicians regarding the potential dangers of prescribing ACE inhibitor, ARB, and/or statin medications to women of childbearing age. Because the use of these targeted medications continues to increase for the management of HTN, DM, and HLD, prescribers need to evaluate evidence-based guidelines in addition to the patient's childbearing status.[1] This study demonstrated that interventions aimed at increasing prescriber awareness of the teratogenic risk associated with targeted medications significantly improved rates of risk documentation for all prescribers (residents and faculty physicians) from 20% before to 37.4% after intervention.

Risk documentation before and after intervention occurred more frequently among women 40 years of age or younger, demonstrating the need to increase awareness of drug exposure with advanced childbearing age. Risk documentation, although occurring more frequently in women 15 to 40 years of age, was suboptimal before and after interven-

tion at 29.8% and 45.2%, respectively. Though improvements in risk documentation occurred in each age category, more than 50% of women with increased fertility may have inadvertent exposure to targeted medications without knowledge of the teratogenic risk.

Additional considerations with this study include that ACE inhibitors were the most frequently prescribed targeted medication, and HTN was the most commonly treated indication both before and after intervention. It is hard to determine from the retrospective chart review if ACE inhibitors or ARBs were prescribed for HTN, DM, or both. If patients with the diagnosis of HTN alone are evaluated, 88 patients (44%) before and 58 patients (44.2%) after intervention could have been prescribed ACE inhibitors or ARBs for HTN alone with no other compelling indication for this drug choice.[2,11] Among women of childbearing age, safer options exist to treat HTN that may not pose a threat to the fetus should pregnancy occur.[11]

This study is similar to the previously published studies and continues to demonstrate the need to improve physician awareness of teratogenic risk when prescribing ACE inhibitors, ARBs, or statins for women of childbearing age.[4,6] Martin and colleagues'[4] study evaluates prescribing in a referral-based HTN clinic, where our study demonstrates prescribing in a primary care setting. Our study also evaluated prescribing and risk documentation among both resident and faculty physicians, finding no difference in the PGY of resident training or faculty physicians. This suggests that increased awareness of prescribing ACE inhibitors, ARBs, and/or statins needs to be reinforced throughout residency training and practice after residency.

There are several limitations to this study that warrant discussion. The demographic data revealed a significant difference in PGY of physician training or faculty physician status from before to after intervention ($P < .001$). This is attributed to the transition of residents into and out of a residency training program each year. Outliers in the data are the PGY1 residents, residents who graduated in 2009, and residents who graduated at other times throughout the study period. The timing of study data collection included the time frame in which PGY3 residents graduated and new PGY1 residents entered training programs. Though there was a statistically significant difference in PGY of training before and after intervention, this did not affect the rate of risk documentation.

Another limitation of this study is rate of prescribed birth control. National statistics reveal that 36.7% of women of childbearing potential use nonpermanent, prescription methods of birth control (ie, oral contraceptive, injectable contraceptive, or intrauterine device).[12] This study evaluated the use of nonpermanent, prescription methods of birth control and revealed that these agents were prescribed to approximately 25% of the before- and after-intervention populations. The lower prescribing rate may be related to the study setting, a Catholic-affiliated institution. The rate of prescribed methods of nonpermanent birth control in this study may not be reflective of the general population.

In addition to these limitations, the survey and the multiple interventions that took place require further discussion. Both before and after intervention, the survey had slightly more than a 30% response rate. Though the response rate received from this survey is in line with expected survey response,[13] the physicians who participated in the survey were not reflective of the physicians prescribing targeted medications. The survey was anonymous; therefore, there was no way to link survey participants to the study prescribers. A majority of the survey respondents were PGY1 family medicine residents. A majority of targeted medication prescribers were internal medicine residents, and PGY1 residents were one of the study outliers because of the influx of new residents entering training. This makes it difficult to correlate the survey results to the frequency of targeted medication(s) prescribed or the rate of risk documentation. Other interventions were present in this study that may have affected the rate of risk documentation, including (1) educational sessions aimed at increasing prescriber awareness when prescribing to women of childbearing age in general and when prescribing targeted medications; (2) implementation of an electronic template for risk documentation when targeted medications were prescribed; (3) memo to physicians with an individualized list of patients who had been prescribed targeted medications; and (4) one-on-one interaction with clinical pharmacy staff through daily prospective chart reviews. Analysis of these interventions revealed that after intervention, 28 of 49 prescribers (57.1%) used the electronic template for risk documenta-

tion and 20 patients had targeted medications discontinued independent of a physician visit. It was not possible to determine which intervention(s) had the greatest impact on improvements in risk documentation and awareness when prescribing after intervention.

Conclusion

Though interventions in this study demonstrate one method to improve awareness of teratogenic risk when prescribing ACE inhibitors, ARBs, or statins in women of childbearing age, there remains room for improvement. Continued efforts to improve prescribing practices and risk documentation at the PCC include second- through fourth-quarter evaluation of data for the remainder of 2010, sharing quarterly data with resident and faculty physicians, providing physicians with individual lists of patients quarterly, encouraging use of the electronic risk documentation template, and yearly review of data with incoming residents. This study demonstrates the continued need to evaluate prescribing practices of physicians for women of childbearing potential while incorporating evidence-based medicine. Identifying patients at risk as well as providing a teratogenic risk discussion and appropriate documentation within the medical record is aimed at reducing potential teratogenic drug exposure.

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