Improving the Safety of Teratogen Prescribing Practices in a Pediatric Rheumatology Clinic

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OBJECTIVES: Although teratogenic medications are commonly used to treat rheumatic disease, no standard model currently exists for educating adolescent patients about teratogenic risk or performing routine pregnancy screening. We performed a quality improvement project to increase education and pregnancy screening in girls and women of childbearing age prescribed teratogenic medications in our pediatric rheumatology clinic.

METHODS: Eligible participants included female patients age 10 and older prescribed teratogenic medications in a single-center tertiary care pediatric rheumatology clinic. Seven plan-do-study-act cycles were completed to test the following interventions: visible project reminders, physician and nurse education, progress updates, previsit planning, and development of an electronic health record education template. Chart reviews were performed, and control charts were created for each aim to analyze improvement over time.

RESULTS: At baseline, 57 of 231 (24.7%) clinic encounters of female patients age 10 years and older taking teratogenic medications had education documented within the last 12 months, and 47 of 231 (20.3%) had pregnancy screening performed at the visit. Implementation of our interventions resulted in improvement in documentation of annual teratogen education (904 of 1135; 79.6%) and routine pregnancy screening (940 of 1135; 82.8%), both of which were statistically significant (P < .0001). Control charts revealed special cause with sustained improvement over >1 year.

CONCLUSIONS: The interventions made through this quality improvement project increased the frequency of both teratogen education and urine pregnancy screening in patients taking teratogenic medications. Development of a standardized education template in the electronic health record played a key role in sustaining these improvements over time.
The American Academy of Pediatrics recommends screening for sexual activity annually, encouraging delayed sexual activity, and providing contraceptive counseling to adolescents who plan to become sexually active. Specific guidelines are lacking for higher risk adolescents, including those taking teratogenic medications. The Food and Drug Administration (FDA)-mandated mycophenolate Risk Evaluation and Mitigation Strategy (REMS) outlines reproductive health guidelines for girls and women of childbearing age prescribed mycophenolate. The REMS mandates education about risks of conceiving while taking mycophenolate and requires pregnancy testing before mycophenolate prescription and at follow-up.

Because many patients with chronic medical conditions perceive their subspecialist as their main doctor, responsibilities for preventive care often shift to the subspecialist. Rheumatologists share responsibility with primary care providers for promoting pregnancy avoidance in patients taking teratogenic antirheumatic medications. Barriers to incorporating reproductive health screening into rheumatology visits include time constraints, clinic logistics, patient discomfort, and provider ambivalence.

The publication of mycophenolate REMS highlighted the need for a standardized approach to prescribing teratogenic medications in our clinic. We conducted this quality improvement project to increase pregnancy screening and teratogen education by applying the mycophenolate REMS practices to all teratogenic antirheumatic medications prescribed.

**METHODS**

**Setting**

This project was conducted in the pediatric rheumatology clinic at Children’s Mercy Hospital, a tertiary care pediatric hospital in Kansas City, Missouri. At the project onset, the clinic was staffed by 5 pediatric rheumatologists and 5 nurses and averaged 3500 visits per year. One additional rheumatologist was hired, and nursing turnover occurred during this project.

**Patients**

Eligible participants included female patients 10 and older (on the basis of hospital pregnancy screening policy) who were seen in the rheumatology clinic from January 2013 to July 2015 and prescribed FDA pregnancy category C, D, or X medications. Most patients were prescribed methotrexate or mycophenolate. Other medications included abatacept, high-dose corticosteroids, cyclophosphamide, cyclosporine, tocilizumab, leflunomide, and rituximab. During the sustainment period from August 2015 to July 2016, ongoing pregnancy screening was stopped in premenarchal patients age 10 to 12 and those taking class C medications after consideration of costs versus benefits in these lower-risk groups.

**Preintervention Work**

Our interdisciplinary project team used the Model for Improvement as the project framework. A key driver diagram was developed to analyze clinic processes and identify potential interventions (Fig 1). On the basis of published barriers to reproductive health education, education and buy in of stakeholders (providers, staff, and patients) and consistent documentation were identified as key drivers. Interventions used to target these drivers were tested through iterative plan-do-study-act (PDSA) cycles.

**Interventions**

Our project team delegated responsibility for initial medication education to the physician and subsequent annual education to the registered nurse. Physicians were tasked with ordering and interpreting pregnancy screening and nurses with sample collection.

During the project, 7 interventions were tested through PDSA cycles (Fig 2). Posters listing teratogenic medications were placed in examination rooms and charting areas to raise project awareness and alert patients to our pregnancy screening efforts.
screening policy. Physicians received education about mycophenolate REMS, the project aims, and the physician’s role. Nurses were taught how to identify patients needing annual education and provide consistent education by using medication-specific scripts. Scripts were developed outlining the medication’s teratogenic risk, measures to mitigate risk, and prompts to offer referral to the teenage clinic for birth control. Project status updates were started at monthly division meetings to maintain project momentum and keep staff engaged. At each meeting, control chart data were discussed with the team.

A preclinic checklist was designed to identify patients eligible for pregnancy screening and education and facilitate preclinic physician-nurse huddles. After several PDSA cycles, the checklist was abandoned because adoption was inconsistent. A standardized template for documenting education discussions in the electronic health record (EHR) was identified as a key intervention early in the project and was implemented after a 1-year development process. This “Rheumatology Patient Education” template allows the physician or nurse to select a medication, review teaching points with a patient, and rapidly and consistently document that discussion in the medical record. When a medication is selected, a box opens revealing 2 sections of scripted educational content: general education and reproductive health. When completed, the template is used to generate an easily locatable document in the EHR containing the date and content of the discussion (Fig 3).

Finally, a formal previsit planning process designed to support multiple quality improvement initiatives was implemented and adopted by all physician-nurse teams. A previsit planning form was created that includes quality initiatives (uveitis screening, medication education and/or pregnancy screening, vaccinations, transition to adult care) and routine clinical care items (laboratories, imaging, social work consult). Before the clinic day, charts are reviewed to identify patients needing annual education or pregnancy screening. Pregnancy screening is reordered for eligible patients. The final step of previsit planning is a physician-nurse huddle immediately before clinic.

A new clinic procedure of documenting last menstrual period in female patients age 10 and older was instituted during the surveillance phase to facilitate restricting ongoing pregnancy screening in girls ages 10 to 12 to those who are postmenarchal.

**Study of the Intervention**

Throughout the project, impacts on clinic flow and patient concerns were assessed through query of staff at monthly division meetings. Only 1 patient refused pregnancy screening on the basis of religious beliefs, and no major impacts on clinic flow were identified.

**Measures**

Because the relevant outcome measure of number of pregnancies is a rare event, the project was primarily focused on process measures for safe prescribing: (1) documentation of teratogen education and (2) pregnancy screening. A sample of charts from 3 representative physicians was reviewed from January 2013 to August 2013 to establish baseline rates of education and pregnancy screening. Because a frequency for follow-up pregnancy screening is not specified in our model (mycophenolate REMS), we approached each clinic encounter as an opportunity to identify pregnancy and mitigate risk of continued teratogenic exposure.5 We obtained pregnancy screening before each infusion for intravenous medications and with each follow-up visit for subcutaneous or oral medications. Pregnancy screening was considered complete if it had been done on the date of the clinic visit or within the previous 30 days because many patients have laboratories before the visit or with IV infusions. Annual education was considered complete if the EHR stated that teratogenic risk or the need to use birth control if sexually active had been discussed in the last 12 months.

Because there were no benchmarks for the process measures, our team set a goal of documenting education and screening for pregnancy in 90% of eligible patients. After meeting that goal, we ceased testing new interventions and began reviewing a subset of charts to ensure sustained improvement. Pregnancies in patients taking teratogenic medications were reported by staff to the project leader. The project leader documented the number of pregnancies, noting medication exposures and pregnancy outcomes (if known), without patient identifiers.

**Data Analysis**

Monthly chart reviews were performed to determine education and pregnancy screening rates. The charts of all female patients age 10...
and older prescribed teratogenic medications were reviewed until project goals were met (from September 2013 to July 2015), then 20% of eligible patient charts per our revised definition were reviewed to ensure sustainability (from August 2015 to July 2016).

χ² analysis was used to compare overall preintervention and postintervention education and pregnancy screening rates. Annotated control charts were created to display process measures over time. Special cause was assessed by the presence of a shift (8 consecutive data points of 1 side of the centerline), a trend (6 consecutive data points increasing or decreasing), or a data point outside of the control limits. The centerline was adjusted if a shift in the data occurred.

**Ethical Considerations**

The Office of Research Integrity at Children’s Mercy Hospital reviewed this project and determined it was not human subject research.

**RESULTS**

During this project, 1366 eligible patient encounters were reviewed. In the 8-month preintervention period, 57 of 231 eligible patient encounters (24.7%) had teratogen education documented, and 47 patient encounters (20.3%) had pregnancy screening performed. Improvements in both process measures were seen with the interventions tested. In the 23 months after the first intervention, 904 of 1135 eligible patient encounters (79.6%) had teratogen education documented, and 940 patient encounters (82.8%) had pregnancy screening performed. Increases in both measures were statistically significant ($P < .0001$).

Control charts revealing change in pregnancy screening and education over time are shown in Figs 4 and 5. For each measure, shifts in the data occurred, leading to the centerline being adjusted. The centerline for
teratogen education increased from 34.7% to 95%, and the centerline for pregnancy screening increased from 31.8% to 95%. A slight trend toward improvement in pregnancy screening was seen before the project formally began, likely related to the recently published mycophenolate REMS. The first data shift for both measures occurred after 3 education-based interventions (teratogenic medication poster, provider education, nurse education), increasing teratogen education from 34.7% to 87.6% and pregnancy screening from 31.8% to 86.2%. After implementation of the Rheumatology Patient Education template and previsit planning, education increased from 87.6% to 95%, and pregnancy screening from 86.2% to 95%. During the sustainment period, rates of education and pregnancy screening were consistently ≥90%.

Three pregnancies were identified after this project began. One patient receiving high-dose corticosteroids (and infliximab) pursued elective termination, one receiving high-dose corticosteroids and mycophenolate delivered a healthy term infant, and one receiving methotrexate was lost to follow-up with unknown pregnancy outcome. In all cases, the pregnancy was identified through our screening process, and the potentially teratogenic medication was stopped immediately. Two had education documented in the previous year.

DISCUSSION

With this project, increased rates of pregnancy screening and teratogenic risk counseling among reproductive-aged female patients prescribed teratogenic medications in a pediatric rheumatology clinic were found. Using quality improvement methods, we designed and tested interventions that produced statistically significant improvements in both aims. Gains were sustained for 1 year after the
new project interventions ceased. The strategies used in this project have implications that reach beyond rheumatology because teratogenic medications are commonly prescribed by other subspecialties.12

The importance of safe prescribing of teratogenic medications has recently garnered attention in pediatric and adult rheumatology. Quality indicators, or evidence-based, measurable processes representing the minimal standard of care, have been developed for several rheumatic diseases. Annual medication toxicity counseling is a quality indicator for systemic lupus erythematosus.13,14 Despite enthusiasm for high-quality medication counseling, safe prescribing, and shared decision-making, good intentions do not easily translate to successful programs. Numerous regulatory requirements and quality initiatives compete for limited clinical time. Key barriers to performing reproductive health screening and other quality indicators include time and lack of a supportive infrastructure, including efficient ways to document counseling in the EHR.8,15,16

Authors of several studies have described approaches to teratogenic medication education for adult patients by using computer-based support.17–19 Although satisfaction was high in patients who received counseling, in 1 study of a computer-based support tool, 43% of women still received no medication counseling.19 Thus, a single intervention may be inadequate to produce significant improvement. Hayward et al20 recently reported the impact of an institutional cyclophosphamide REMS protocol on pre cyclophosphamide pregnancy screening. With their approach, they produced dramatic improvement in pregnancy screening and highlighted the challenges to fostering lasting
change in a dynamic setting. With our project, we similarly aimed to implement a comprehensive strategy but extended the scope to all teratogenic medications.

It is challenging to assess the impact of the individual interventions in this project. The cumulative effect of multiple targeted interventions likely led to the sustainable improvement seen. It is suggested in reliability science that educational interventions alone are unlikely to produce sustained change when human factors are involved. Checklists, reminders, and standardized processes are more effective but alone have not ensured consistent provision of medication education in other studies. After initial improvement with staff educational sessions, we designed subsequent interventions to produce ongoing improvement and enhance sustainability.

An early iteration of previsit planning (ie, our preclinic checklist) was abandoned because of inconsistent use because it was perceived by team members as an extraneous task in the setting of a busy clinic. Buy in was poor regarding the impact previsit planning would have on performance and clinic efficiency. A more comprehensive previsit planning process was successfully implemented later as part of a global shift in our clinic’s approach to quality improvement and task allocation. The new process had higher staff buy in because it was used to address multiple quality improvement projects and hospital requirements, some linked to provider remuneration. The previsit planning process has been modified iteratively, including changes in planning form content and division of responsibilities. Initial parallel clinic preparation by physicians and nurses was redundant and led to each role eventually taking “ownership” of certain aspects of previsit planning. Although the process has evolved over time, previsit planning is now part of standard clinical care in our practice.

Although a way of documenting education discussions in the EHR was identified as a priority, it was clear that development would be time consuming. In tandem with that work, we pursued simpler interventions that resulted in early improvements in both process measures. Early gains achieved through staff education and project progress reports were sustained through previsit planning and development of a standardized EHR documentation template. Through significant collaboration with the information technology department, the Rheumatology Patient Education template was implemented. This novel EHR template provides both a standardized location for documentation of education discussions and scripting to ensure patients receive consistent, accurate educational content from all rheumatology clinic staff. Since implementation, the nurses have assumed responsibility for ongoing teratogen education and maintained the improvements seen with initial project interventions. Development of an electronic template helped streamline our documentation process in a system reliant on an EHR; however, effective interventions need not be complex or computer based. The success of previsit planning in our clinic by using a paper checklist highlights that simple interventions implemented consistently can impact change. Paper checklists including scripting for education discussions could be used in settings without EHRs.

These results should be viewed in the context of several potential limitations. The ideal approach to safely prescribing medications with teratogenic potential is not well defined, particularly in adolescents. Extending mycophenolate REMS concepts to other medications depended on judgments by the project team about which medications to target, the definition of “childbearing age,” and frequency of pregnancy screening. Initially, we included medications classified as C, D, or X in the former FDA pregnancy risk system. Other authors have described educational interventions and pregnancy screening targeting class D and X medications. After project goals were attained, the team discussed future directions for the surveillance phase. Because pregnancy in our population is a rare event, the cost of regular pregnancy screening was thought to outweigh the benefit in patients taking class C medications. Patients prescribed a class C medication continued to receive counseling using scripting reflecting what is known about that medication’s pregnancy risk. During this project, the FDA Pregnancy and Lactation Labeling Rule replaced lettered risk categories with descriptive labeling about risks in pregnancy, lactation, and individuals of reproductive potential. Highlighted in this change is the importance of tailoring reproductive health counseling to individual medications, which we found practical to implement using EHR template scripting.

At the project onset, girls were considered of childbearing age after age 10 on the basis of a pregnancy screening policy approved at our institution in 2010. There is not a universally accepted definition of childbearing age in adolescents. The American College of Radiology defines the lower limit of menstrual age as 12 in their practice parameter for imaging potentially pregnant patients. During the sustainment period, we discontinued ongoing pregnancy screening in premenarchal girls ages 10 to 12 after a consideration of costs of repeated screening in that low-risk population. Ethical considerations in this age group include limited patient
understanding, which leads to consent for this sensitive testing being parent-driven, and the legal implications of a positive test result.

Several factors extrinsic to our interventions may have impacted our results. A new provider joined our practice, and we experienced significant nursing turnover, although those changes might be expected to diminish rather than enhance improvement. An overall increased focus on quality improvement in our division may have affected outcomes beyond the impact of previsit planning.

The successful implementation of medication counseling and pregnancy screening in our patient population has potential implications for pediatric rheumatology and other pediatric subspecialties. The structure and content of our EHR education template has been shared with other divisions in our hospital and pediatric rheumatology divisions at other institutions with the same EHR. Ultimately, the improvement seen was not the result of a single intervention but of a comprehensive change in the way teratogenic medications are managed in our clinic. Keys to success were consistent project leadership by an invested interdisciplinary team, participant engagement and buy in, and support from an institutional leadership invested in quality improvement.

CONCLUSIONS

Because the optimal approach to safe prescribing of teratogenic medications in adolescents is not established, strategies used to reduce risk from fetal exposure to teratogenic medications prescribed in the pediatric rheumatology clinic are needed. Through development of a divisional protocol for prescribing teratogenic medications and serial interventions to improve staff compliance with the protocol, we increased teratogenic medication education and pregnancy screening in our clinic. Tools developed during this project have been shared with other specialties and other institutions. Additional work would be required to assess whether spread of these tools has produced similar results in other settings and whether our patient education efforts led to increased patient understanding of teratogenic risk and changes in risk behaviors.

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ABBREVIATIONS

EHR: electronic health record
FDA: Food and Drug Administration
PDSA: plan-do-study-act
REMS: Risk Evaluation and Mitigation Strategy

REFERENCES


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