A Clinical Case of Electronic Health Record Drug Alert Fatigue: Consequences for Patient Outcome

abstract

Despite advances in electronic medication order entry systems, it has been well established that clinicians override many drug allergy alerts generated by the electronic health record. The direct clinical consequences of overalerting clinicians in a pediatric setting have not been well demonstrated in the literature. We observed a patient in the PICU who experienced complications as a result of an extended series of non-evidence-based alerts in the electronic health record. Subsequently, evidence-based allergy alerting changes were made to the hospital’s system. Incorporating clinical evidence in electronic drug allergy alerting systems remains challenging, especially in pediatric settings. Pediatrics 2013;131:e1970–e1973

AUTHORS: C. William Carspecken, MSc, MBA, Paul J. Sharek, MD, MPH, Christopher Longhurst, MD, MS, and Natalie M. Pageler, MD

Department of Biomedical Informatics, Stanford University, Stanford, California; Harvard Medical School, Boston, Massachusetts; Center for Quality and Clinical Effectiveness, Lucile Packard Children’s Hospital, Palo Alto, California; and Divisions of General Pediatrics, Systems Medicine, and Critical Care Medicine, Department of Pediatrics, Stanford University School of Medicine, Stanford, California

KEY WORDS: electronic health record, drug allergy, alert fatigue, pediatrics, clinical decision support systems, override, quality improvement, adverse drug event

ABBREVIATIONS

ADE—adverse drug event
CDSS—clinical decision support systems
EHR—electronic health record

Mr Carspecken wrote, compiled, and revised the primary and final drafts; Drs Sharek and Longhurst provided revisions and feedback; and Dr Pageler drafted, revised, and provided final approval for the manuscript.

www.pediatrics.org/cgi/doi/10.1542/peds.2012-3252
doi:10.1542/peds.2012-3252

Accepted for publication Jan 30, 2013

Address correspondence to Natalie M. Pageler, MD, Center for Excellence in Pulmonary Biology, Division of Pediatric Critical Care Medicine, Stanford University School of Medicine, 770 Welch Rd, Ste 350, Stanford, CA 94304. E-mail: npageler@stanford.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275). Copyright © 2013 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

COMPANION PAPER: A companion to this article can be found on page e1948, and online at www.pediatrics.org/cgi/doi/10.1542/peds.2013-0864.
Although adoption of electronic health records (EHRs) with integrated computerized clinical decision support systems (CDSS) has decreased hospital errors and risks to patients,\textsuperscript{1,2} the optimal technological implementation of these systems remains elusive. One such area of concern is how to best alert physicians of allergy-induced preventable adverse drug events (ADEs) when entering drug orders electronically,\textsuperscript{3} especially for pediatric patient populations for whom drug allergy prevalence varies substantially from adults.\textsuperscript{4} An important subset of preventable ADEs frequently targeted by CDSS is drug allergy cross-reactivity; however, a paucity of evidence regarding the efficacy of such alerts in practice remains.\textsuperscript{5} A barrier to effective alerting systems is the large number of inappropriate alerts, leading to widespread override of medication alerts by providers. Clinician overrides of drug allergy alerts in settings, such as the Department of Veterans Affairs,\textsuperscript{6} tertiary medical centers,\textsuperscript{7} and outpatient ambulatory clinics,\textsuperscript{8} demonstrate that between 69% and 91% of alerts are overridden. Most allergy alerts do not provide clinically significant information that alters the clinician’s care because the alerts are based on unlikely potential cross sensitivities or on incorrectly entered allergy data.\textsuperscript{7} This situation creates far too many false-positive alerts,\textsuperscript{9} which leads to alert fatigue. More than a mere nuisance for health care providers, alert fatigue has been defined as “declining clinician responsiveness to a particular type of alert as the clinician is repeatedly exposed to that alert over a period of time, gradually becoming ‘fatigued’ or desensitized to it.”\textsuperscript{10} Electronic alert fatigue renders CDSS less effective and presents a serious patient safety issue,\textsuperscript{11} as demonstrated by a recent clinical case in the PICU at Lucile Packard’s Children’s Hospital.

**PATIENT PRESENTATION**

A 2-year-old boy with a history of short gut syndrome due to gastroschisis, total parenteral nutrition–associated cholestasis, status post liver, and small bowel transplantation 5 months prior was admitted to the PICU with respiratory distress and rash of unclear etiology. Although he had a documented sulfonamide antibiotic allergy in the EHR, he required treatment with both chlorothiazide and furosemide during the course of his inpatient hospitalization. Each time the 2 diuretics were indicated and administered during the hospitalization, alerts based on potential drug allergy cross reactivity would be generated, as shown in Fig 1. The clinical team overrode those alerts based on strong evidence suggesting that cross-reactivity of these medications is not the basis for hypersensitivity.\textsuperscript{12} The various clinical staff that appropriately ordered and administered this patient’s medications overrode more than 100 alerts over a 1-month time frame. During the hospital course, the patient’s rash became exfoliating and more extensive, eventually involving more than 60% of his body surface area. Dermatology, plastics, and allergy/immunology services were consulted. Based on the results of a skin biopsy, the primary differential diagnosis for the rash was a drug hypersensitivity reaction versus graft-versus-host disease. Given the concern for a true allergic hypersensitivity to furosemide, a furosemide allergy was documented in the record in addition to the preexisting sulfonamide antibiotic allergy. Desensitization to EHR drug alerting by the deluge of overrides, however, resulted in temporary continued administration, over the course of 1 night, of the now inappropriate furosemide medication. This event complicated the evaluation and treatment of his worsening, desquamating rash.

Based on the differential diagnosis, the patient’s immunosuppression was increased to treat possible graft-versus-host disease and further allergy studies were pursued. A basophil activation assay was performed on the patient’s blood against sulfonamide drugs. This test revealed that he did not have...
a Type I immunoglobulin E–mediated hypersensitivity allergic response to sulfonamide. However, this test did not rule out allergic reactions to sulfonamide metabolites or either Type III or Type IV hypersensitivities to sulfonamide medications. Given the patient’s worsening clinical status, clinicians decided to cautiously administer several sulfonamide-containing medications (both antimicrobial agents and diuretics). He appeared to tolerate these medications well with continued positive response to his immunosuppressive regimen, suggesting that he did not, in fact, have allergy to the medications. Unfortunately, the patient eventually died after developing fungal pneumonia with subsequent respiratory failure and septic shock.

**DISCUSSION**

Although the patient’s clinical course was complicated by many factors, the inappropriate allergy overrides further confused the situation. The solution to the problem of drug allergy alert overrides and the ensuing alert fatigue encompasses many sociotechnical aspects of clinical health systems, such as ensuring provider education on how to document allergy, incorporating evidence-based medicine into health information systems, and unifying medication allergies into a single digital location. Implementing clinical evidence-based drug cross-reactivity rules into health information systems, rather than relying on pharmacologic moiety-driven databases, poses several important challenges. These databases come built into the software of many vendor-based EHR systems and are often unchanged to accommodate new clinical evidence. The terminology and true incidence of substance intolerance, especially in pediatric medicine, lacks clarity in many respects. Moreover, the time-dependent nature of adverse drug reactions makes data-driven prediction of effects challenging, although there has been significant recent progress. Excessive electronic alerts warning clinicians of potential but rare adverse drug cross reactions result in increased patient safety risks by rendering these alerts meaningless. The challenge of omitting specific drug cross-reactivity pairings from CDSS raises appropriate questions of ensuring proper sensitivity for detection of true allergy-based ADEs. Careful consideration to eliminate medication pairings alerts that pose a minimal theoretical risk of true hypersensitivity is critical. This was done at Lucile Packard’s Children’s Hospital as a result of this clinical case to ensure adequate attention is paid to legitimate alerts. Staff physicians, pharmacists, and informaticists worked with the EHR vendor to modify and improve the allergy alerting system. These enhancements included a streamlined approach to allergy entry, distinguishing between allergy alerts for sulfonamide antibiotics and nonantibiotics, enhanced alerts to nursing staff, and staff education. Turning off improper alerts in practice has been challenging, as a direct result of variation in physician drug-related knowledge and hospital drug-monitoring routines. Uncertainty about drug reaction severity, legal concerns, and regulatory mandates with public reporting implications further complicate implementation of smarter alerting systems.

From a malpractice perspective, the creation of a tort “safe haven” would rightly recognize that experimentation with evidence-based CDSS software systems could protect both clinicians and software vendors in an overall effort to improve patient safety. Although new international guidelines designed to identify the most important drug warnings could assist this process, regulation and rigorous evaluation of clinical information systems are by no means one and the same. As recently remarked, the payoffs of information technology investment come only after intensive process reengineering, a formidable task in the pediatric setting.

**CONCLUSIONS**

As the medical community increasingly embraces clinical decision support tools and electronic drug order entry safeguards, there must be a heightened awareness of overalerting risks to patient well-being. The threat of missing a rare event must be balanced with the dangers of burdening clinicians with unnecessary and interruptive electronic alerts. True evidence-based medicine must rely on risk mitigation on both sensitivity and specificity fronts if the full potential of health information technology can be realized. Analogous to ICU alarm fatigue, this article shows the clinical consequences of EHR alert fatigue on patient health.

**REFERENCES**


A Clinical Case of Electronic Health Record Drug Alert Fatigue: Consequences for Patient Outcome
C. William Carspecken, Paul J. Sharek, Christopher Longhurst and Natalie M. Pageler
*Pediatrics* 2013;131:e1970; originally published online May 27, 2013;
DOI: 10.1542/peds.2012-3252

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th>including high resolution figures, can be found at: /content/131/6/e1970.full.html</th>
</tr>
</thead>
<tbody>
<tr>
<td>References</td>
<td>This article cites 21 articles, 8 of which can be accessed free at: /content/131/6/e1970.full.html#ref-list-1</td>
</tr>
<tr>
<td>Citations</td>
<td>This article has been cited by 17 HighWire-hosted articles: /content/131/6/e1970.full.html#related-urls</td>
</tr>
<tr>
<td>Subspecialty Collections</td>
<td>This article, along with others on similar topics, appears in the following collection(s):</td>
</tr>
<tr>
<td></td>
<td>Dermatology /cgi/collection/dermatology_sub</td>
</tr>
<tr>
<td></td>
<td>Administration/Practice Management /cgi/collection/administration:practice_management_sub</td>
</tr>
<tr>
<td></td>
<td>Quality Improvement /cgi/collection/quality_improvement_sub</td>
</tr>
<tr>
<td></td>
<td>Health Information Technology /cgi/collection/health_information_technology_sub</td>
</tr>
<tr>
<td></td>
<td>Electronic Health Records /cgi/collection/electronic_health_records_sub</td>
</tr>
<tr>
<td>Permissions &amp; Licensing</td>
<td>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: /site/misc/Permissions.xhtml</td>
</tr>
<tr>
<td>Reprints</td>
<td>Information about ordering reprints can be found online: /site/misc/reprints.xhtml</td>
</tr>
</tbody>
</table>

PEDiATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2013 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.
A Clinical Case of Electronic Health Record Drug Alert Fatigue: Consequences for Patient Outcome
C. William Carspecken, Paul J. Sharek, Christopher Longhurst and Natalie M. Pageler

Pediatrics 2013;131:e1970; originally published online May 27, 2013; DOI: 10.1542/peds.2012-3252

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/131/6/e1970.full.html