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Towards a Clinical Decision Support System for Drug Allergy Management: Are Existing Drug Reference Terminologies Sufficient for Identifying Substitutes and Cross-Reactants?

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Abstract

Drug allergy cross-reactivity checking is an important component of electronic health record systems. Currently, a single, open-source medication dictionary that can provide this function does not exist. In this study, we assessed the feasibility of using RxNorm and NDF-RT(National Drug File – Reference Terminology) for allergy management decision support. We evaluated the performance of using the Pharmacological Class, Mechanism of Action and Chemical Structure NDF-RT classifications in discriminating between safe and cross-reactive alternatives to a sample of common drug allergens. The positive predictive values for the three approaches were 96.3%, 99.3% and 96.2% respectively. The negative predictive values were 94.7%, 56.8% and 92.6%. Our findings suggest that in the absence of an established medication allergy classification system, using the Pharmacologic Class and Chemical Structure classifications in NDF-RT may still be effective for discriminating between safe and cross-reactive alternatives to potential allergens.

Keywords:

Drug Allergy; Terminology; Clinical Decision Support.

Introduction

A key function of a medication allergy decision support system is the ability to discriminate between the safe-to-use substitutes and cross-reactants of medication allergens. The NDF-RT (National Drug File – Reference Terminology) and RxNorm are two publicly available terminology standards for the electronic representation of drug information. The NDF-RT contains different hierarchies that are used to categorize medications [1]. RxNorm provides normalized names for clinical drug-related concepts [2]. In this study, we investigate the feasibility of using the two resources in identifying safe substitutes and cross-reactants of common drug allergens.

Methods

We identified the RxNorm ingredient concepts of twelve drugs: Aspirin, Atorvastatin, Cephalexin, Clarithromycin, Doxycycline, Enalapril, Enoxaparin, Ibuprofen, Losartan, Morphine, Penicillin G and Sulfasalazine. For each ingredient concept identified, we extracted the mappings to NDF-RT and generated the sets of ingredients with the same Indication, Pharmacologic Class, Mechanism of Action and Chemical Structure. Three set-theory-based criteria were applied to discriminate between safe and cross-reactive alternatives to the twelve ingredients studied. By the Pharmacologic Class criteria, the safe alternatives to an ingredient used for a particular indication was defined as the set of ingredients with the same Indication (A) but different Pharmacologic Class (B) i.e. $\{x \in A | x \notin B\}$. Conversely, cross-reactants were identified as the set of ingredients with the same Pharmacologic Class (B) i.e. $\{x \in B\}$. The same logic was applied to the Mechanism of Action and Chemical Structure criteria. We evaluated the ability of each criterion to correctly identify the sets of safe alternatives and cross-reactants against a gold standard derived from medical literature.

Results

The sensitivity, specificity, positive predictive value and negative predictive value of the three criteria are shown in Table 1. All three criteria had high positive predictive values, suggesting that they are good at correctly identifying true safe alternatives. The Pharmacologic Class and Chemical Structure criteria had high negative predictive values, suggesting that they may be good at correctly identifying true cross-reactants.

Table 1: Performance of Criteria used to discriminate between select safe (S) and cross-reactive (CR) medications

		Reference		% SEN	% SPE	% PPV	% NPV
		S	**CR**				
PC	S	988	38	99.5	70.1	96.3	94.7
	CR	5	89				
MOA	S	901	6	90.7	95.3	99.3	56.8
	CR	92	121				
CS	S	986	39	99.3	69.3	96.2	92.6
	CR	7	88				

S: Safe, CR: Cross-reactive, SEN : Sensitivity, SPE: Specificity, PPV : Positive Predictive Value, NPV: Negative Predictive, PC: Pharmacology Class, MOA: Mechanism of Action, CS: Chemical Structure

Conclusion

Our findings demonstrate the feasibility of using the NDF-RT and RxNorm to infer safe and cross-reactive medications in the absence of an established medication allergy classification system, with the caveat that a more generalizable approach would require additional curation. Different criteria may be selectively be applied to particular situations.

References

[1] NDF-RT Documentation. Available at http://evs.nci.nih.gov/ftp1/NDF-RT/NDF-RT%20Documentation.pdf. Accessed December 19, 2014.

[2] RxNorm Documentation. http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#. Last Accessed December 19, 2014.

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