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# Detecting Drug-Adverse Event Safety Signals through Quantitative Data Mining of MEDLINE Indexing Terms: A Pilot Study.

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**Background**: FDA conducts postmarketing drug safety surveillance by analyzing spontaneous adverse event (AE) reports submitted to the FDA Adverse Event Reporting System. In this pilot study, we assessed the feasibility of detecting drug-AE safety signals in the use case of the fluoroquinolones (FQ) by systematic data mining of MEDLINE indexing terms.
**Methods**: By leveraging the Medical Subject Heading indexing terms assigned to MEDLINE reports, we extracted associations between co-occurring drug entities (in the context of adverse effects or concomitant) and chemically-induced clinical manifestations. We computed statistical associations (adjusted signal scores [SS]) for every drug-AE pair by estimating adjusted relative reporting ratios with confidence intervals. A large set of known adverse drug reactions and negative controls was used to validate the performance of the data mining methods from the extracted data.
**Results**: We identified 113 unique FQ class-AE pairs from a structured output of 354,692 MEDLINE reports and 446,227 drug/drug class-AE pairs. The top adjusted SSs for FQs were tendinopathy, tendon rupture, torsade de pointes, long QT, and pseudomembranous colitis, AEs included in FQ drug labels. The highest adjusted SSs for tendinopathy within all drug-AE pairs occurred with FQs, Collagenases, and HMG-CoA Reductase Inhibitors with the FQs having an adjusted SS of over 400 times higher than expected given the extracted data (table). Due to the nature of the analysis and the MEDLINE data, the adjusted SSs do not indicate causality or absolute risk for the associations.

| **Drug Class** | **Number of Articles** | **Adjusted Signal Scores (SS) with 90% CIs** |
|---|---|---|
| Fluoroquinolones | 46 | 476 (367-598) |
| Collagenases | 9 | 187 (97-299) |
| HMG-CoA Reductase Inhibitors | 5 | 16 (6-29) |

**Conclusions**: In this pilot study, we detected safety signals for known toxicities of the FQs and other drugs by data mining of MEDLINE indexing terms. Future research will assess various signal detection algorithms and seek to integrate MEDLINE with other data mining streams as part of a comprehensive approach to pharmacovigilance.