Evaluation of Adverse Event Sampling Bias

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Abstract

As Americans consume increasingly complex combinations of drugs, dietary supplements, and herbal remedies, the capacity for adverse events to attribute to interactions between these agents will be magnified. Adverse event reporting systems may help identify clinicians’ perceptions and expert judgments about interactions stems from the use of anecdotal adverse event reports to evaluate drug and dietary supplement safety. The broad-based collection of information concerning adverse events from drugs and supplements is the FDA-sponsored voluntary reporting system, which does not provide a representative sample of adverse events in the population. We have evaluated the literature on adverse event reports with respect to the statistical tools that might be used to assess adverse event prevalence and incidence, and the inaccuracies that can be drawn from these tools. We find at least two underlying sources of bias inherent in the statistical tests when using non-random sampled data. First, adverse event reports for specific toxicities are often recruited through advertising, producing a database of adverse event reports shown to be more frequent in uncontrolled, public awareness and worse, is vulnerable to reporting of adverse event reports as influenced by specific interests in a particular adverse event. It is not uncommon for adverse event reports (AERs) and case reports. A retrospective study found this system was able to identify 20 of 30 known adverse events 1-5 years sooner than conventional epidemiologic studies with adequate power. The data collected are most often incomplete and inferior in quality, with a large number of errors and limitations. Reporting rates could be influenced by factors that do not alter incidence. The data collected are most often incomplete and inferior in quality, with a large number of errors and limitations. Reporting rates are not incidence rates.

Introduction

Sources of Drug Interaction Information:

• Pre-clinical: During drug development the probability of drug interactions is based on structure-function assumptions. In clinical trials patients with multiple medications are often excluded limiting the ability to detect drug interactions.
• Post-marketing: Drug interactions are evaluated using adverse event reports (AERs) and case reports. The FDA’s database of adverse events comes from voluntary reporting by consumers and health care providers (approx. 10%) and mandatory reporting by manufacturers. Over 300,000 reports annually.\b
• FDA uses a data-mining algorithm designed to detect unexpected adverse drug events and some drug-drug interactions in the databases. \c When combinations of clinical events and medications are disproportionately present in the databases, an association is suspected.

Rationale & Methods

Publicity on Health is Abundant. Sources:

• Print
• Internet
• Print Media

Adverse Event Information Via Internet

• Commercial news organizations
• Academic & commercial medical information websites
• Commentary on web blogs
• Personal & Legal Attorneys

Expectation: Surge in AER frequency precedes publicity. Preliminary Observation: Publicity occurs before peak of AERs. Hypothesis: Publicity may influence AER frequency.

Method:

2. Searched FDA AER database from 2000 - 2006 (Q1 & Q2).
3. Compared publicity with FDA AER database by year.

Conclusion:

• The analysis conducted here cannot be considered a scientific investigation due to the inability to verify, measure and control key influences on AERs: use of AERs to make inferences about drug and dietary supplement safety suffer the same limitation.
• The influence of publicity on AER incidence would need to be measured and controlled for allowed to use AERs to evaluate the relative safety of drugs or dietary supplements.

Conclusions

• Publicity about adverse drug effects may precipitate dramatic increases in adverse event reporting, suggesting that publicity may profoundly affect AER incidence via reporting bias.
• Publicity may promote AE reporting at months or years after drug administration.
• Because adverse events are anecdotal and uncontrolled, reporting of AERs after drug use may be subject to recall bias.
• Until extraneous influences on AER incidence can be measured and controlled, little useful information can be gleaned regarding potential adverse interactions between drug-drug or drug-supplement combinations; even reliable hypothesis generation would be difficult given current uncertainties.

References