Web-based data tool designed to enhance drug safety

July 8 2016

A new online open-access database has been developed by scientists to allow the clinical responses of more than 5 million patients to all FDA-approved drugs to be used to identify unexpected clinical harm, benefits and alternative treatment choices for individual patients, according to a study appearing July 8 in *Nature Biotechnology*.

Developed by scientists in the Division of Biomedical Informatics and the Clinical and Translational Sciences Program at Cincinnati Children's Hospital Medical Center, the database has the potential to help reduce negative side effects from prescription drugs and identify opportunities to reposition existing drugs for new uses, report the study's authors.

Calling their new database AERSMine, researchers said the tool allows anyone from physicians to the general public to rapidly find, combine and analyze the growing volume of drug information stored in the U.S. Food and Drug Administration's Adverse Reporting System (FAERS).

"AERSMine offers an open aperture approach that can reveal unexpectedly better or worse clinical outcomes associated with different drug regimens for some groups of patients, and to facilitate the ultimate goal of protecting patients by improving therapeutic selections and monitoring strategies," said Mayur Sarangdhar, PhD, study first author and a research associate in the Division of Biomedical Informatics at Cincinnati Children's. "It also conserves valuable therapeutics by minimizing harmful interaction choices."

Although the FDA's database offers an extensive array of reports and related data on the clinical use of drugs and adverse effects, study authors said that current methods for information retrieval and analysis are difficult -running the risk of losing statistical power and the ability to detect important differential effects.

AERSMine is designed for easy use and supports analysis of millions of clinical records containing details on drug exposures, disease indications, and clinical outcomes. Researchers said the tool is expected to strengthen access to and analysis of drug safety and effectiveness data. It also has the potential to discover improved uses of individual drugs or drug combinations and develop novel treatments for diseases.

"One of the capabilities that makes AERSMine different from any other clinical data mining system is its ability to use knowledge frameworks - ontologies -to form the groupings of patients, medications, and outcomes and gain what we believe is an unprecedented power to explore and identify both unexpectedly negative and positive drug effects. Doing this has the potential to uncover new uses for drugs and drug regimen combinations," said Bruce Aronow, PhD, senior study author and co-director of the Computational Medicine Center at Cincinnati Children's.

Using the database

The researchers evaluated the effectiveness and utility of the data mining tool by running a series of analyses involving both known side effects as well as more complex scenarios focused on improved use of three important classes of drugs and clinical disorders: 1) lithium - used to treat manic depression/bipolar disorder; 2) anti-tumor necrosis factor (anti-TNF) drugs - used to treat inflammatory conditions such as rheumatoid arthritis; 3) NSAIDs - non-steroidal anti-inflammatory drugs used for pain management.

Their analysis of lithium, for example, showed that 22,575 patients had used lithium with a total of 4,180 adverse drug events. AERSMine-dissected data shows that 327 adverse events significantly correlated with patients that use lithium, including aggression, anger, suicidal tendencies, tremors, irritability, etc., have a significantly reduced rate of occurrence in patients taking angiotensin receptor blocks (ARBs, usually taken to control hypertension). The intriguing possibility suggested by AERSMine analysis then is that ARBs could result in a reduction of these sometimes lethal outcomes of bipolar patients taking lithium.

When the authors studied the use of NSAIDs for arthritis, chronic pain, etc., they were able to see differential rates of adverse clinical events depending on if people used propionic acid derivatives (like ibuprofen) or so-called cox-2 inhibitors known as coxibs, and patient groups for whom the risks of NSAID adverse events are much lower than others (for example patients with chronic arthritis).

"Next generation functions of AERSMine, and part of what we believe provides its underlying power is based on the functions of networks of genes that link the co-occurring clinical phenotypes and drug mechanisms of action to the functions of biological systems," said Anil Jegga, DVM, MRes, study co-author and a computational biologist in the Division of Biomedical Informatics. "This allows the molecular basis for drug-related adverse events to be detected, leveraged, and used to identify opportunities for repositioning drugs for new clinical uses."

More information: AERSMine is accessible at: research.cchmc.org/aers/

Provided by Cincinnati Children's Hospital Medical Center