Off-label prescription drug use and adverse drug events

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Off-label use of prescription drugs was associated with adverse drug events in a study of patients in Canada, especially off-label use lacking strong scientific evidence, according to an article published online by *JAMA Internal Medicine*.

Off-label prescribing of drugs is common and has been identified as a potentially important contributor to preventable adverse drug events (ADEs).

Tewodros Eguale, M.D., Ph.D., of McGill University, Montreal, Canada, and now of MCPHS University (Massachusetts College of Pharmacy and Health Sciences), Boston, and coauthors looked at the off-label use of prescription drugs and its effect on ADEs in 46,021 patients who received 151,305 prescribed drugs from primary care clinics in Quebec, Canada. Electronic health records documented treatment indications and outcomes. Prescriptions dispensed from 2005 through 2009 were followed up and examined. The authors looked at off-label prescription drug use with and without strong scientific evidence.

The authors identified 3,484 ADEs in the 46,021 study patients. The overall incidence rate of ADEs for all drugs was 13.2 per 10,000 person-months. The rate of ADEs for off-label use (19.7 per 10,000 person-months) was higher than for on-label use (12.5 per 10,000 person-months), according to the results.

Off-label use that lacked strong scientific evidence had a higher ADE

rate (21.7 per 10,000 person-months) compared with on-label use and off-label use with strong scientific evidence (13.2 per 10,000 person-months) had about the same risk for ADEs as on-label use, the study reports.

The risk for ADEs grew as the number of prescription drugs the patient used increased, according to the authors. For example, patients using eight or more drugs had more than a 5-fold increased risk for ADEs compared with patients who used one to two drugs.

The authors note a number of study limitations, which include missed medication-related symptoms by physicians and patients who don't tell physicians about all their symptoms. The study also did not measure the cost of ADEs.

"Off-label drug use, and particularly off-label use without strong scientific evidence, is a risk factor for ADEs. Hence, physicians and physician organizations should recognize the enormity of the problem and be active participants in the promotion of cautious prescribing of drugs for off-label uses lacking strong scientific evidence. Future EHRs should be designed to enable postmarketing surveillance of treatment indications and treatment outcomes to monitor the safety of on- and off-label uses of drugs," the authors conclude.

In a related commentary, Chester B. Good, M.D., M.P.H., and Walid F. Gellad, M.D., M.P.H., of the Veterans Affairs Pittsburgh Heathcare System, write: "Egulae and colleagues have provided compelling evidence that off-label prescribing is frequently inappropriate and that prescribing in these circumstances increases the risk for an adverse event substantially. The FDA and the courts must carefully consider these findings as they contemplate guidance that would relax regulations to permit promotion of drugs beyond their labeled indications."

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