Adverse Drug Events: Implications For Prescribing Psychotropic Medications

John L. Caccavale, Ph.D., M.S. (Clinical PsychoPharmacology)
Jack G. Wiggins, Ph.D., ABPP

Abstract

Medication errors may result in over 100,000 deaths and 650,000 injuries with an annual cost exceeding $172 billion dollars. Prescriber errors are frequently cited as the predominant causes of serious adverse drug errors (ADEs). Lack of pharmacology training in medical school may be a contributing factor to medication errors. Thus medical school training alone may be insufficient for safe prescribing. Although data show that psychotropic medications may be safer than other classes of medications and produce far fewer injuries and fatalities, specialized training may be required for this class of drugs as well. ADE awareness is recommended for inclusion in psychopharmacology training.

Introduction

The American Psychological Association (APA) Council's decision to seek prescriptive authority (RxP) for psychologists trained in psychopharmacology has led to statutory successes in the jurisdictions of Guam, New Mexico and Louisiana. Continued opposition by psychiatry and medicine to prescribing by psychologists argues that medical school training is necessary to prescribe psychotropic medications safely. Psychologists opposed to prescriptive authority also focus on the patient safety issue.[1,2] Psychologists who support RxP equally are concerned about patient safety.[4,5,6] Prescribing errors may result in adverse drug events ADEs. ADEs are defined as harms, both serious and minor, to patients. Prescribing errors include prescribing the wrong dose of a medication or prescribing the wrong medication or using the wrong route of administration. Given that errors in prescribing medications are common, analysis of medication errors has important implications for both prescribing psychologists and programs that train them.

Adverse Drug Events: Drug Costs And ADE Incidence Rates

During the calendar year ending 2001 over three billion prescriptions for medications were written in the United States at a cost well over $132 billion dollars[7,8,9] projects this cost to rise to over $400 billion by the year 2014. Recent passage of a prescription benefit bill is likely to greatly increase these costs. The growing use and reliance on prescription medications presents American society with major health, public safety, and public policy dilemmas. The helpfulness and efficacy of many prescribed medications is unarguable. When used appropriately for the conditions

indicated, pharmaceuticals can contribute to the quality of life. On the other hand, prescribed medications are not without risk.

Estimates of the annual cost due to increased harm from medication related injuries ranges from a low of $72 billion to a high of $172 billion.[7] The fact that the increased harm and costs from medications may actually exceed the total annual cost of medications themselves begs for further study. Fatalities from adverse drug events in the United States are estimated to exceed 100,000 people on a yearly basis. [10] Annual non-fatal injuries from ADEs are estimated to be about 650,000.[10,11] These statistics are alarming but they only represent fatalities and harm to those patients in hospital settings. Data for ambulatory patients is sorely lacking due to a lack of an enforceable policy for systematically reporting ambulatory ADEs.

It is important for all healthcare professions to be knowledgeable regarding adverse drug events associated with prescription medications. Psychology**,** as a health care profession**,** is no exception. Knowledge of ADEs is particularly important for those psychologists seeking prescriptive authority. Knowledge on the types and incidence rates of ADEs also can shed light on whether a medical school training is a necessary prerequisite to safely prescribe medications as argued by opponents of non-physician prescribers. Medical studies have long been concerned with patient safety related to the use of medications.[12,13] The Harvard School of Public Health conducted one of the first studies to look at ADEs associated with prescription medications.[14,15] This Harvard benchmark study was a first attempt at trying to quantify the types and incident rates of medication errors in a large population of hospitalized patients. In a sample of over 30,000 hospitalized patients, they concluded that medication errors were associated with serious

outcomes that negatively affected patient safety. Overall, they found that adverse events from medications comprised about 20% of total errors**.**

All prescription medications approved by the US Food and Drug Administration (FDA) are for specific purposes. Most medications are of little use outside their stated purpose although many medications are used "off label" with little or no data to support their use.[16] Cardiovascular, gastrointestinal, endocrinological, antibacterial and hematological drugs are examples of medications that have little or no use for conditions other than purposes for which they are approved. These classes of medications comprise the greater share of fatalities and serious ADEs.[17,18,19]

The FDA delineates two types of drug related adverse events. Type A ADEs are harms resulting from prescription medication errors and other avoidable errors. Harms can range from a simple and minor rash to death. Type B ADEs are harms not related to errors but to the unique response of the patient to the drug, e.g., anaphylactic shock. "Undetected hypersensitivity or unknown inherited response to a medication" comprise this category of ADEs. Table 1 presents findings from four major studies representing the type and incidence of avoidable medication errors that affect patient safety. The four studies cited were selected because they are representative of the types of studies typically encountered in the ADE literature and are among the most frequently cited.

Table 1 About Here

. The above citations, besides being representative of ADEs studies, are presented because they additionally show route errors, which are missing in many ADE studies. The types of errors described in the above studies seem to change very little from year to year.[20,21] Prescribing of the wrong dose or the wrong medication even when known allergies to a medication exist, is a major problem. Overdosing is another serious problem. When errors such as these occur time and again, chance occurrence is not a viable explanation.[22] In response to the escalating ADE problem, many hospitals have implemented ADE reduction programs such as utilizing pharmacists to review physician medication orders. Review of physician orders by pharmacists in order to provide medication counseling on all new prescriptions is now required by Medicare. This federal requirement has resulted in pharmacists being granted limited prescriptive authority in over 40 states. Many of these prescription review programs have reduced ADEs associated with the types of errors presented in the cited studies.[23,24] There are many variables that can explain ADEs, e.g., physician distraction, workload, unfamiliarity with a specific medication. Specific training on ADE pitfalls in all pharmacological training is recommended for safe prescribing.

The Institute of Medicine (IOM) of the National Academies of Sciences did a comprehensive investigation of medical errors and published this landmark study as To Err Is Human (2000).[10] One of the major findings of that study was that annual fatalities from medication errors surpassed deaths from motor vehicle accidents (43,458), breast cancer (42,297), and AIDS (16,516). Many of the findings and conclusions of this study, however, have been challenged.[25,26,27] Generally,

these studies dispute the both the incident rate and seriousness of ADEs cited in the IOM study. Acknowledging that some of the findings on ADEs may be overstated, the IOM study sheds much light on the risks associated with current prescribing practices in medicine.

Classes Of Medicines Most Related To Injury And Harm To Patients

Opiate and cardiac medications contribute the greater share of all ADEs and fatalities.[28,29] Available data suggests that the risks of ADEs associated with psychotropic medications may be far less than those of drugs used for other disorders.[30,31] Table 2 presents data comparing the frequency of ADEs by medication class. Although the data shown in Table 2 is over 10 years old, the more recent studies presented in Table 3 are generally are consistent with the earlier studies. Psychotropic medications are related to far less ADEs than other classes of medications.

Table 2 About Here

In the year ending 2000, over 16,000 deaths from gastrointestinal complications were attributed to non-steroidal anti-inflammatory drugs.[19] In addition, several thousand more deaths involving cardiovascular complications also were attributed to this same class of medication, which are used to treat common inflammation.[18] Increasingly, we see psychotropics being used for conditions they are not approved for and with populations never intended. Psychotropic drugs are often used by managed care organizations as a less costly substitute for psychotherapy. Weight

loss, dermatological problems, student behavioral control, autism, inappropriate behavioral restraint, podiatry, pain management, and in dentistry, are examples of applications not indicated by research or, in many cases, by logic. Antidepressant medications are being prescribed for an ever- expanding catalog of newly created problems.[32,33] Uses of these medications, like many medications, go beyond those initially indicated and their use becomes more questionable. Newer atypical antipsychotic medications, for example, are finding even greater use for non-psychotic conditions such as insomnia, and with children[34] that are populations generally excluded from drug trials. Although the incidence rates of injury and hepatotoxicity from psychotropic drugs are relatively low, psychologists must remain alert to the hazards of ADEs when prescribing. ADE incident rates can be a reality check even though there is mounting evidence that psychotropic medications may be relatively safer when compared to other classes of medications. Greater risk to patients from psychotropic medications occurs when these types of medications are prescribed by medical professionals who are not specifically trained in clinical psychopharmacology and in the diagnosis of mental disorders.[35]

An analysis of ADE studies, including fatalities, associated with psychotropic medications shows that psychotropic medications may be among the safest of all classes of medications.[36,37,38] These studies show that opiates, cardiovascular and noon-steroidal anti-inflammatory drugs (NSAID) medications comprise the greatest share of serious ADEs. These classes of medications are not an objective of psychologists seeking prescriptive authority. In comparison, since its introduction several years ago, the anti-psychotic medication Clozaril, a drug used to treat schizophrenia in a population of treatment resistant patients, registers about 10-15 fatalities for every 10,000 patient years.[39] This is a very low incidence rate in comparison to fatalities resulting

from NSAIDs and other medications despite its higher potential for ADEs among all psychotropic medications. The intention here is not to minimize the potential harms that can result from the inappropriate use of psychotropic medications. When ADEs do arise from the use of psychotropics, they can be attributed to use with the wrong populations, errors in the prescriptions[10] and to the inherent uniqueness in response of the patients receiving them. Data with respect to ADEs associated with particular classes of medications is scarce and incomplete. A few studies have provided some insight into the classes of drugs most associated with ADEs in hospitalized and outpatient settings. Table 3 presents data on ADEs by drug class and medication. The two studies are almost equivalent with respect to the classes of medications contributing to the most frequent occurrences of ADEs.

Table 3 About Here

Is Medical School Training The Most Effective Way To Reduce Prescribing Errors?

Steel [40] argues that many ADEs are related to limited medical training in pharmacology and calls for physicians to be licensed to prescribe medications only in their specialty. Wiggins & Cummings [41] reported 1 million episodes of mental health care where psychologists with documented training in psychopharmacology managed both the combined use of psychotherapy

and psychotropic medications without patients' complaints of how psychologists dealt with their medications. Several studies of the effectiveness of prescribing psychologists in the military show that they perform safely and with high standards.[42] These data suggest that the greatest danger to patients may not be a function of who prescribes but the content and quality of training one gets to learn how to prescribe.[43,44,45] Thus, the available data do not support a broad assertion that only a medical school education can prepare health professionals to prescribe safely.

Training Recommendations

All prescribers need to go beyond medical schools' more limited training experiences in pharmacology by focusing greater attention on preventable ADEs. Given what we know about many of the causes of ADEs, specific training recommendations can easily be implemented to significantly reduce Type A ADEs. One positive recommendation would be to provide training in drug-drug interactions between drug classes. With over 7000 medications now in use, it is almost impossible to recall specific drug-drug interactions between single medications. Since most medications in a class behave similarly, this could reduce ADEs. For example, generally, non-steroidal medications (NSAIDS) can have serious drug-drug interactions with antihypertensives. Knowing this can alert prescribers to this interaction and would require a more detailed look into specific drugs that are being considered in these classes.

We now have available very detailed, but easy to use, computerized pharmacology programs. Rx Epocrates is an example of such a program. These programs are easy to update and take very little time to master. In cases where multiple medications are being used, performing a simultaneous drug-drug interaction search can take seconds. Pharmacology programs should train in their use and require students to acquire and use this technology.

Many ADEs occur due to prescribers writing an incorrect dose of a medication. For example, medications, such as Levoxyl, a thyroid hormone substitute, must be prescribed in *microgram* doses. This drug is responsible for a significant number of ADEs, with serious consequences, simply because the prescriber writes the dose as *milligrams*. Reducing this type of ADE can be accomplished simply by providing training in dosing arithmetic similar to that required of nurses and physical assistants. Along this line, ADEs related to writing errors, where bad hand writing is the causative factor, can be significantly impacted by eliminating hand written prescriptions. Students who are trained from the beginning to order prescriptions in type will tend to utilize this method when they gain authority to prescribe.

Training programs would do well to integrate the practice of writing mock prescriptions into their training. Case studies now comprise an important part of training. Requiring students to provide typed mock prescriptions, as opposed to on-the-fly recommendations, for these case studies, can provide the overt and latent learning important to later prescribing. Practice can make perfect. Clearly, prescribing medications requires skills that must start with early training. As in many professions, there are those who may lack the skills needed to correctly and competently perform tasks.[46] Training that addresses ADEs is not prominent and included in the core subject matter of the majority of medical schools.[47] While this type of training may not guarantee the competence of any one prescriber, without specific training in ADEs, we may invite only more ADEs and their subsequent consequences. Prescribing psychologists can be in the unique position of being a positive factor in reducing ADEs while at the same time providing mental health services effectively and efficiently. General practitioners and other non-psychiatric physicians are neither mental health specialists nor psychopharmacologists. Steel [40] commenting

on a recent study on ADEs [48] advocates that non-physicians and sophisticated computer systems need to be part of the prescribing process if ADEs are to effectively be controlled.

Concluding Statements

Collaboration between non-physician prescribers and physicians can result in more effective and safer treatment for mental health patients by reducing ADEs. By adding a thorough knowledge of ADEs to pharmacological training, psychologists can promote higher quality mental health care, while increasing access to services 2002). with better treatment efficiency and reducing overall health care costs.[6,49,50] The Therapy in America Survey [51] reports that an estimated 59 million people received some form of mental health treatment in the last two years. However, an estimated 24 million people received no treatment even though they reported having symptoms severe enough to warrant a diagnosis and treatment.

Patients experiencing depression and seeing a general practitioner are often undiagnosed or misdiagnosed. McGynn [52] reports that only 53% of patients with depression receive a adequate standard of care and their symptoms go untreated or they are given medications for something that they may not even need. Misdiagnosis, inappropriate medications, insufficient training in mental disorders, and poor pharmacology skills, can all increase the likelihood of ADEs. Suicide rates among people who are not being seen by a mental health professional are several times greater than those patients receiving treatment.[53,54] Psychologists can fill a significant gap in mental health care by prescribing psychotropic medications and providing related psychological services. Prescribing psychologists will need continuing education in ADE prevention as they acquire additional experience in reading and interpreting medication research studies to avoid organized medicine's ADE experiences.

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Table 1

Commonly studied medication errors as causes of adverse drug events (ADEs):

Percent of ADEs for each cause

Note: A 'Route Error' pertains to the method of delivery of a medication i.e., by mouth, injection, IV.

Study: Bates, Boyle & Vander Vliet, (1995). Relationship between medication errors and adverse drug events. *J Gen Intern Med* ,10,199-205.

Dosing error: 31.0%
Known allergy: 4.0%
Wrong drug/patient: 4.0%
Route error: 10.0%

Study: Leape, Bates & Cullen, (1995). Systems analysis of adverse drug events. *JAMA*, 274, 35-43.

Dosing error: 28.0%
Known allergy: 8.0%
Wrong drug/patient: 9.0%
Route error: 2.0%

Study: Lesar, Briceland & Stein, (1997). Factors related to errors in medication prescribing. *JAMA*, 277,312-7.

Dosing error: 58.3%
Known allergy: 12.9%
Wrong drug/patient: 5.4%
Route error: 3.3%

Study: Thomas, Studdert & Newhouse,(1999). Costs of medical injuries in Utah and Colorado. *Inquiry*, 36, 255-64.

Dosing error: 7.9%
Known allergy: 5.7%
Wrong drug/patient: 20.9%
Route error: 4.0%

Table 2
Classes of Drugs Commonly Responsible for Adverse Effects*

Antibiotic agents
Chemotherapeutic agents
Anticoagulant agents
Cardiovascular agents
Anticonvulsant agents
Antidiabetic agents
Antihypertensive agents
Analgesic agents
Antiasthma agents
Sedative-hypnotic agents
Antidepressant agents
Antipsychotic agents
Antiulcer agents

*--Listed in order from most frequent to less frequent.

Adapted from Leape LL, Brennan TA, Laird N, Lawthers AG, Localio AR, Barnes BA, et al. The nature of adverse events in hospitalized patients. Results of the Harvard Medical Practice Study II. N Engl J Med 1991;324:377-84.

Table 3
Adverse Drug Events by Medication Class. And Medication.

Study: Gurwitz J.H., Field T.S., Harrold L.R., Rothschild J, Debellis, K, Seger A.C., Cadoret, C., Fish, L.S., Garber, L., Kelleher, M., Bates, D.W. (2003). Incidence and preventability of adverse drug events among older persons in the ambulatory setting. JAMA., Mar 5, 289,9, 1154-6.

Medication Class	Number of ADEs	Percent of Total
Cardiovasculars	526	34.5
Diuretics	337	22.1
Nonopioid analgesics	233	15.4
Hypoglycemics	167	10.9
Anticoagulants	155	10.2
Neuropsychiatrics	105	6.9
	N=1523	

Study: Winterstein, J., Hatton, R.C., Gonzalez-Rothi, R, Johns, T.E., & Segal, R.(2002). Identifying clinically significant preventable adverse drug events through a hospital's database of adverse drug event reports. *Am J Health Syst Pharm*, 15, 1742-1749.

Medication	Number of ADEs	Percent of Total
Warfarin (Anticoagulant)	736	47.3
Heparin (Anticoagulant)	98	6.3
Morphine (Opiate)	221	14.2
Meperidine (Opiate)	50	3.2
Insulin (Anti-Hyperglycemic)	171	11.0
Midazolam (Benzodiazepine)	87	5.6
Digoxin (Cardiac)	56	3.6
Phenytoin (Anti-Seizure)	56	3.6
Cyclosporine (Immunosuppressant)	40	2.6
Promethazine (Anti-Nausea)	40	2.6
	N=1555	
