The Pharmacist Activist

Volume 17, No. 2 • February 2022

"But the wisdom that comes from heaven is first of all pure, then peace-loving, considerate, submissive, full of mercy and good fruit, impartial and sincere." James 3:17

Editorial

Medication Errors - If the Public Knew. . .

how many medication/dispensing errors occur, they would be outraged! It has been almost 25 years since the comprehensive report, *To Err is Human: Building a Safer Health System*, was published by the Institute of Medicine (IOM) in 1999. It is *estimated* in the report that as many as 98,000 Americans die every year from medical errors that occur in hospitals. As alarming as this statistic is, it is noteworthy that the estimate only represents deaths of patients who are hospitalized, and not those who survived the harm of a medical error or the vast majority of individuals who are not hospitalized. In addition to errors resulting from incidents such as incorrect diagnoses, mistakes during surgeries, and health care-acquired infections, medication/dispensing errors are also common among these preventable tragedies. Medication errors can be errors of commission that occur as a result of the wrong action taken, or omission that occur as a result of actions not taken.

The FDA receives more than 100,000 reports every year that are associated with medication errors, and it has been estimated that 7,000 to 9,000 Americans die each year as a result of a medication error. However, data are often unconfirmed, unreliable, incomplete, and vary widely. To the extent that agreement exists among those who are concerned about medication errors it would be in the recognition that adverse experiences of those taking medications are often attributed to explanations (e.g., worsening of the underlying medical problem) other than the use of a medication, medication errors are usually not reported and, therefore, are known only to those who are directly involved, and that the consequences and number of medication errors are deserving of urgent attention. It has been suggested by some that *medical* (including medication) errors are the third leading cause of death in the United States, following heart disease and cancer. However, in sharp contrast to the deaths from heart disease and cancer, there are not reliable data to support the estimates of deaths resulting from medication errors. The incompleteness, unreliability, and confusion, regarding the data in the Vaccine Adverse Event Reporting System (VAERS) regarding the use of COVID-19 vaccines, represent a current example of the challenge of reporting and recording information with respect to the use of just one type of medical product.

Following the "wake-up call"

The IOM report in 1999 was widely viewed as a wake-up call to urgently and effectively address the tragic consequences of medical errors, and more than enough time has elapsed to assess the response of health professionals and society. On a positive note, pharmacist Michael Cohen and his colleagues at the Institute for Safe Medication Practices (ISMP) have continued and expanded their exemplary advocacy and programs to increase the awareness of medication errors and initiatives to reduce them. As with the IOM report, a guiding principle for ISMP is that the problem is *not* bad people in health care but is that good people are working in bad systems that need to be made safer. A limited number of other individuals and organizations have also committed significant effort to address these problems.

It was anticipated by many that the widespread adoption of electronic prescribing would substantially reduce the number of errors attributable to misinterpretation of poorly legible handwritten prescriptions.

Contents

Although this is a forward step, it does not avoid what one pharmacist has designated "neat mistakes" when a printed, legible product name other than the one intended is entered and transmitted to a pharmacy. As one example, I was recently asked to serve as an expert witness in a lawsuit brought by a woman who is highly allergic to aspirin who experienced serious harm when an aspirin–containing product was mistakenly prescribed instead of an acetaminophen-containing alternative listed next to it.

Since 1999 there have also been situations that have increased the possibility of medication errors. Thousands of new prescription and nonprescription medications, as well as dietary supplements, have been marketed, many of which have serious risks and some of which have names that are similar to those of other products. The increasing number, properties, and complexities of these products further add to the practice challenges experienced by pharmacists and to the risk of errors.

It is my strong belief that the most important factor with respect to the occurrence of medication errors is the greatly increased extent to which pharmacies are owned by individuals or corporations who are not pharmacists and/or otherwise are not committed to giving a high priority to the effective and safe use of medications. This situation is most evident in the community setting in which many independent pharmacies have closed or have been acquired by large chain pharmacies, but also is apparent in the ownership and operation of mail-order pharmacies and hospital/healthcare system networks. The operations of these corporations are driven by economic factors, and the quality and safety of healthcare services and medications are secondary considerations at best. With greatly increasing frequency, pharmacists do not have the autonomy or authority for policies, staffing, and other decisions that result in understaffed, stressful, and error-prone workplace conditions that are now so prevalent. If pharmacists even raise concerns, they are often at risk of termination. A highly probable consequence is an increase in medication errors, and I would contend that, since 1999, the profession of pharmacy has *regressed* rather than *progressed* in the prevention of medication errors.

Who should be responsible?

With respect to the use of medications, is there anything more important than the avoidance of errors? Can there be any question that it should be individual pharmacists and the profession of pharmacy that have the greatest responsibility in preventing medication errors? How can we explain our failures in not substantially reducing their occurrence, or even being able to provide reliable information with respect to their frequency?

Individual pharmacists on the front lines in practice settings must be more responsible and accountable. Our pharmacy organizations must do much more to support these pharmacists by exposing and challenging the corporations, systems, policies, and individuals that are responsible for the problems that presently exist. Those of us who do not have direct responsibilities in serving patients must do much more on behalf of patients and our profession in increasing awareness of medication errors and actions needed to avoid them.

A response that a corporation dispenses billions of prescriptions and that the percentage for which there are errors is miniscule and can be anticipated is disingenuous and must be rejected. A denominator of 1 billion prescriptions and a claim of a 0.001% error rate represents a numerator of 10,000 actual patients who experienced an error. The settlement of a lawsuit that alleges a medication error must not be interpreted that an error did not actually occur or there was not wrongdoing despite a refusal to acknowledge such.

State Boards of Pharmacy exist to regulate the practice of pharmacy in a manner that provides residents of the state with as much assurance as possible regarding the effectiveness and safety of their medications. They have the authority to take disciplinary/remedial actions against pharmacists and pharmacies when justified. I am aware of positive initiatives in California and Illinois to address the working conditions and other factors that often are associated with medication errors. To what extent are such initiatives being taken in your state?

Recommended action

The inertia with respect to the reduction of medication errors is inexcusable. A system must be established in which all serious medication errors must be reported to the board of pharmacy in the states in which they occurred, and it is remarkable that so little has been done in this direction and that there are few, if any structured reporting systems in place that would be of value for protecting patients as well as better preparing pharmacists for avoidance of errors. Perhaps the limitations with respect to the amount, types, and unreliability of information that is presently available regarding medication errors have been barriers in even considering the development of programs that would acquire and provide for pharmacists information and guidance that would be of value. However, information is available, although not currently accessible, that would provide a strong foundation on which a more comprehensive reporting system and error avoidance programs could be established.

Together, CVS, Walgreens, Walmart, and Rite Aid own more than 25,000 pharmacies. All or most of the executives and other decision makers in these corporations are not pharmacists and, as a consequence, the autonomy, authority, and decision-making prerogatives of the pharmacists most directly involved with customers are severely compromised. Each of these companies, however, requires detailed documentation of errors that occur in its stores, if for no other reason than to evaluate employee performance and potential disciplinary measures.

For the primary purposes of acquiring definitive information regarding the types and frequency of medication errors, as well as the

(Continued on Page 4)

New Drug Review

COVID-19 Nirmatrelvir/ritonavir (Paxlovid – Pfizer)

Description:
A SARS-CoV-2 main protease inhibitor; with ritonavir, an HIV-1 protease inhibitor and CYP3A4 inhibitor.

Indication:
Emergency Use Authorization (EUA): Administered orally for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

Limitations of use: Is not authorized for initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19, for pre-exposure or post-exposure prophylaxis for prevention of COVID-19, or for use longer than 5 consecutive days.

New Drug Comparison Rating (NDCR) = 4
(significant advantages) in a scale of 1 to 5 with 5 being the highest rating

Comparable drugs:
Bamlanivimab/etesevimab, casirivimab/imdevimab (REGEN-COV), sotrovimab.

Advantages:
- Is the first orally-administered antiviral product to be demonstrated to be effective in the treatment of COVID-19;
- Has a different mechanism of action that may provide effectiveness against more variants of SARS-CoV-2.

Disadvantages:
- Interacts with many other drugs;
- Use is not recommended in patients with severe hepatic or severe renal impairment;
- Use is limited to patients 12 years of age and older (compared with bamlanivimab/etesevimab which may be used in patients as young as newborns);
- Authorized use is more limited (compared with bamlanivimab/etesevimab and casirivimab/imdevimab that are also authorized for use for post-exposure prophylaxis for prevention of COVID-19).

Recommended dosage:
Nirmatrelvir must be co-administered with ritonavir, with which it is co-packaged; 300 mg (two 150 mg tablets) with 100 mg ritonavir (one tablet) with all three tablets taken together twice daily for 5 days; treatment should be initiated as soon as possible after diagnosis of COVID-19, and within 5 days of symptom onset; dosage of nirmatrelvir should be reduced by one-half in patients with moderate renal impairment.

Products:
Co-package of nirmatrelvir film-coated tablets (150 mg) and ritonavir film-coated tablets (100 mg).

Contraindications/most important risks:
- Interactions: Concurrent use of Paxlovid is contraindicated with drugs that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions (alfuzosin, meperidine, piroxicam, propoxyphene, ranolazine, amiodarone, dronedarone, flecainide, propafenone, quinidine, colchicine, lurasidone, pimozide, clozapine, dihydroergotamine, ergotamine, methylergonovine, lovastatin, simvastatin, sildenafil (when used for PAH), triazolam, oral midazolam);

  Concurrent use of Paxlovid is contraindicated with drugs that are potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir concentrations may be associated with the potential for loss of virologic response and possible resistance (carbamazepine, phenobarbital, phenytoin, rifampin, St. John's wort, apalutamide);

  EUA fact sheet should be consulted regarding additional medications with which Paxlovid may interact;
- Hepatic adverse events (e.g., transaminase elevations, jaundice).

Most common adverse events:
Dysguesia (6%), diarrhea (3%), hypertension (1%), myalgia (1%).

Comments:
Nirmatrelvir inhibits the SARS-CoV-2 main protease (Mpro) and prevents viral replication. Ritonavir is not active against SARS-CoV-2 Mpro, but inhibits the CYP3A-mediated metabolism of nirmatrelvir, resulting in increased plasma concentrations of the latter agent. Paxlovid was evaluated in a placebo-controlled trial in non-hospitalized adults, in which COVID-19 related hospitalization or death from any cause through Day 28 was 0.8% (no deaths) in Paxlovid-treated patients (n=1039), and 6.3% (1.1% deaths) in patients receiving placebo (n=1046).

Daniel A. Hussar

(cont. - Medication Errors)

provision of error avoidance educational programs for pharmacists, state boards of pharmacy should require these four chain organizations to provide the reports/records of serious medication errors that have been experienced by patients in their respective states. The names of patients and the pharmacy personnel involved can be redacted from the reports, as can the identification/location of the specific pharmacy within the state to protect the anonymity of those involved. Records for the period from January 1, 2021 to date should be requested and immunity should be provided by the board against further investigation and action with respect to events in these records that have already occurred. The organizations would subsequently be required to provide such reports/records on a monthly basis for monitoring and appropriate follow-up by the board of pharmacy.

It can be anticipated that these chain organizations will adamantly resist providing this information but, with anonymity for individuals and the location of the pharmacy as well as immunity against investigation with respect to events that have already occurred, what legitimate reasons can be provided to not supply the information requested that will be of great value in reducing medication errors?

These four chains will claim they are being singled out and discriminated against and that any information they provide will not provide a complete and accurate analysis of medication errors because the data do not include information from other chain pharmacies, independent pharmacies, hospital pharmacies, long-term care facilities, and other practice settings. The response is that these four organizations currently have the largest amount of pertinent information available that can be evaluated and applied on as timely a basis as possible to reduce the occurrence of medication errors. This is but the first and most efficient step in an initiative that will be subsequently extended to include pharmacies in other practice settings.

Daniel A. Hussar
danandsue3@verizon.net

Oral Antivirals for COVID-19 – We Must Learn from Experience

Through its Emergency Use Authorization (EUA) process, the FDA has enabled the availability of two new antiviral products, nirmatrelvir/ritonavir (Paxlovid – Pfizer) and molnupiravir (Merck) for the treatment of mild to moderate COVID-19 in patients with positive results of direct SARS-Co-V viral testing and who are at high risk for progression to severe COVID-19, including hospitalization and death. Paxlovid is more effective than molnupiravir and is preferred to the latter agent unless there are important risks (e.g., interactions with numerous other drugs) that preclude its use. In some respects, the actions and use of these two new products are analogous to those of oseltamivir for the treatment of influenza virus infection. Specifically, treatment is most effective when it is initiated as soon as possible after diagnosis and within 5 days of symptom onset. Because oseltamivir requires a prescription, the delay incurred for this to be accomplished may reduce the effectiveness of the treatment. Requests to the FDA to permit the availability of oseltamivir without a prescription from a pharmacist have been ignored.

The availability of Paxlovid in particular is important enough to be included in President Biden's State of the Union message which includes the following statements:

> "We are also ready with anti-viral treatments. If you get COVID-19, the Pfizer pill reduces your chance of ending up in the hospital by 90 percent. I've ordered more pills than anyone in the world has. Pfizer is working overtime to get us a million pills this month and more than double that next month. And now we're launching the "Test to Treat" initiative so people can get tested at a pharmacy and, if they prove positive, receive the antiviral pills on the spot at no cost."

This is an excellent initiative but several provisions are essential if this program is to be optimally effective for as many patients who can benefit:

1. Paxlovid and molnupiravir must be available without a prescription from a pharmacist.
2. The distribution and availability of these products must include independent pharmacies as well as large chain pharmacies.
3. The federal government must provide an equitable fee for the services of pharmacists.

Daniel A. Hussar
danandsue3@verizon.net

Author/Editor/Publisher – Daniel A. Hussar, Ph.D.
Dean Emeritus and Remington Professor Emeritus at
Philadelphia College of Pharmacy
Assistant Editor – Suzanne F. Hussar, B.Sc. (Pharmacy)

The Pharmacist Activist, 1 Boulder Creek Lane, Newtown Square, PA 19073
E-mail: info@pharmacistactivist.com

Distribution/Design Services provided by Jeff Zajac