The Pharmacist Activist

Volume 11, No. 11 • November 2016

Editorial

You Say Adherence and I Say Compliance –

Whatever We Call It, Pharmacists, with Our Patients, Must Respond to this Challenge!

I have had a strong and long-standing interest in the subject of patient compliance and published my first paper, "Patient Noncompliance," on this topic in 1974 in the *Journal of the American Pharmaceutical Association*. Numerous speaking and publishing opportunities followed as health professionals became increasingly concerned about the extent and consequences of the situations in which patients were not using prescribed medications in the manner intended.

I can't think of this topic without also thinking of the exceptional and extensive work of Pharmacist Dorothy Smith in addressing the challenge of patient compliance and developing excellent patient education materials. Dorothy is the Founder and President of the Consumer Health Information Corporation and has done more than any other pharmacist or other health professional over a period of several decades in identifying the importance of the consequences of noncompliance and providing recommendations for improving compliance.

It was at a symposium on the topic of compliance that then-Surgeon General Everett Koop made the obvious, but often overlooked declaration, "Drugs don't work if people don't take them." – a statement that ranks among the most frequently quoted observations about medications.

Some examples of noncompliance are almost humorous:

- Patients have chewed and swallowed suppositories because they did not understand that they should be administered rectally.
- Patients have retrieved and cleaned the matrix shells of certain extended-release tablets they have discovered in their feces and concluded that the medication was never released.
- A patient was observed to have dozens of nitroglycerin transdermal patches on his skin on his return appointment with his physician. He correctly applied one patch a day, but no one had said anything about removing them.

However, other examples have very serious and even fatal consequences:

- Patients have experienced rejection of organ transplants because they were noncompliant in using immunosuppressant medications such as cyclosporine.

- Patients have discontinued taking potentially life-prolonging anticancer drugs because of the adverse events experienced.
- Noncompliance with antitubercular regimens over a period of many months has so often resulted in relapses of the infection that the strategy of "directly-observed treatment" is often employed.

From these and many other examples, I have learned to never assume that patients will understand and follow the instructions that will result in the appropriate use of their medications. This statement might suggest that patients are the ones "at fault" when noncompliance occurs. However, although there are some situations in which patients are intentionally noncompliant, noncompliance occurs far more often because patients have not been provided with adequate instructions, or do not understand the instructions that health professionals consider to be clear. For example, the instruction to take one tablet three times a day may seem very specific to a physician and pharmacist, and certainly preferable to "take as directed." However, should the patient take the medication three times a day with meals, every 8 hours, or on some other schedule? For some medications, it will make an important difference.

We should be able to assume that all health professionals have an awareness of noncompliance and its consequences. Some have conducted research studies to document the extent of compliance, others have developed excellent patient education materials, and some have implemented successful strategies in their individual practices that have resulted in improved compliance. These initiatives are commendable and of value, but have not become the standard of practice. Indeed, more often we learn of studies and commentaries that describe abysmally low compliance rates with medications such as antihypertensive drugs and lipid-regulating agents such as the statins.

Compliance or adherence?

Initially, "compliance" was the term that was well understood and almost always used in discussions of patient usage of medications, with terms such as "adherence," "persistence," and "concordance" used on occasion. However, the identification of sociobehavioral determinants and other factors thought to influence how patients use medications resulted in some concluding that "compliance" might be interpreted as coercive and may not be "patient-friendly." Accordingly, some recommended that "adherence" be the preferred term, although many who use this term also perceive a need to define it. I continue to prefer and use the term "compliance" without feeling any guilt or need to define it, but I will concede that the proponents for "adherence" have succeeded in making it the most widely used term.

While some pharmacists and other health professionals become preoccupied with the semantics, the consequences of noncompliance not only continue, but worsen for some patients. Every several years health professionals seem to rediscover the scope and importance of the problem but, notwithstanding some positive but isolated experiences, we have not effectively addressed this challenge in a substantive manner. On the occasions when this problem commands our attention, it is usually not because of concerns for the health and safety of patients, but rather because of the huge dollar costs associated with noncompliance. I admit that it is such a report that has prompted my writing this commentary.

The latest estimated cost

The story headline that most recently captured my attention reads,"Nonadherence costs pharma $600B plus in annual sales" (by Beth Snyder Bulik). Yes, B is for billions! The estimate of $637 billion includes $250 billion of lost revenues in the United States. This amount does not even include the additional costs for the healthcare system to manage the consequences of noncompliance, or the cost in health outcomes for patients. I have not reviewed the methodology or specific parameters of the study that produced these cost statistics but such estimates often use data for a relatively small number of individuals that are then extrapolated to apply to the entire population. As a result, some conclude that the costs identified are unreliable estimates that are not credible. However, even if we consider an amount of $250 billion to be a wild exaggeration and reduce the amount a thousand-fold to only $250 million, consider what could be accomplished with just that amount to achieve positive medication outcomes.

Compliance strategies

Various strategies have been employed to improve compliance including special packaging of prescription medications (e.g., oral contraceptives), printed materials with diagrams and illustrations, and devices that provide a signal or other reminder that it is time for the patient to take the next dose of medication. These initiatives are of value for some, but

(Continued on Page 4)

New Drug Review

Lifitegrast (Xiidra – Shire)
for Dry Eye Disease

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

Indication:
For ophthalmic use for the treatment of the signs and symptoms of dry eye disease.

Comparable drugs:
Cyclosporine ophthalmic emulsion (Restasis).

Advantages:
- Is the first agent to be approved for the treatment of both the signs and symptoms of dry eye disease (whereas cyclosporine is indicated to increase tear production);
- Has a unique mechanism of action (is a lymphocyte function-associated antigen-1[LFA-1] antagonist);
- May have a faster onset of action (improvement may be experienced within several weeks of initiation of treatment whereas the full benefit of cyclosporine may not be experienced for several months).

Disadvantages:
- May cause dysgeusia.

Most important risks/adverse events:
None.

Most common adverse events:
(at an incidence of 5% to 25%) Instillation site irritation, decreased visual acuity, dysgeusia.

Usual dosage:
One drop in each eye twice a day, approximately 12 hours apart, using a single-use container that should be discarded after using in each eye.

Product:
Ophthalmic solution – 5% (50 mg/mL) in single-use containers; patients who wear contact lenses should remove them prior to administration, and they may reinsert them 15 minutes following administration.

Comments:
Dry eye disease is associated with inflammation of the ocular surface and, in addition to eye dryness, symptoms may include eye stinging, burning, or other discomfort, a gritty feeling, and blurred vision. It is usually a chronic disease and, if it becomes severe and is left untreated, pain, corneal ulceration, and scars may result. It is often treated with artificial tears products but many individuals do not experience an adequate response. Other agents that have been used in ophthalmic formulations include corticosteroids, hydroxypropyl cellulose (e.g., Lacrisert ophthalmic insert), and cyclosporine. Lifitegrast is the first medication to be approved for the treatment of both the signs and symptoms of dry eye disease. In contrast, cyclosporine ophthalmic emulsion is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca.

The inflammation associated with dry eye disease is thought to be primarily mediated by T-cells and associated cytokines. This process may be initiated by the increased expression of intercellular adhesion molecule-1 (ICAM-1) in corneal and conjunctival tissues. ICAM-1 interacts with integrin lymphocyte function-associated antigen-1 (LFA-1), a cell surface protein. The LFA-1/ICAM-1 interaction can contribute to the occurrence of an immunological response that stimulates T-cell activation that leads to inflammation of the ocular surface. Lifitegrast is an integrin antagonist that binds to integrin LFA-1 and blocks its interaction with ICAM-1. It is classified as a LFA-1 antagonist and it is thought to reduce the secretion of inflammatory cytokines.

The effectiveness of lifitegrast was evaluated in four 12-week vehicle-controlled studies that involved more than 1,000 patients. The assessment of symptoms was based on a change from baseline in patient-reported eye dryness score (EDS) and, in all four studies, a larger reduction in EDS was observed with lifitegrast. In two of the four studies, an improvement in EDS was observed in two weeks following initiation of treatment, an onset of action that appears faster than that experienced with cyclosporine ophthalmic emulsion, although the two agents have not been directly compared in clinical studies. The assessment of signs was based on inferior corneal staining score (ICSS) using fluorescein. At week 12, a larger reduction in ICSS favoring lifitegrast was reported in three of the four studies.

Daniel A. Hussar

studies continue to show high rates of noncompliance. Some pharmacies have prepared automatic refills of maintenance medications for chronic conditions, although questions have been raised as to whether this approach is motivated to provide benefit for patients or to increase revenue by dispensing more prescriptions.

It is my strong opinion that the *only* strategy that will greatly improve patient compliance is for health professionals to commit more time for face-to-face discussions with individual patients. Such discussions will demonstrate the sincere interest of health professionals in wanting patients to understand the benefits and limitations of their medications, as well as the instructions that will result in their most appropriate use. Questions from patients should be requested so that any uncertainties may be clarified. The personal communication should not end when the prescription is dispensed as there should be follow up discussions to assure appropriate understanding and continued use of the medications in the manner intended.

I recognize that what I am advocating will require a much greater commitment of the very value commodity of our TIME. My recommendation does not correspond with the reality of the practice settings in which many physicians are expected to see more patients per hour/day, and many pharmacists are employed in environments with "more prescriptions faster" metrics and "sign here" patient pickup of prescriptions that often involve no discussion between the patient and pharmacist. However, these situations are not working and are at the expense of patient harm and great cost. We must not tolerate a continuation of these experiences that are eroding the quality of health care.

The concept of medication synchronization as proposed and implemented by Pharmacist John Sykora is an excellent approach that increases meaningful communication with patients and monitoring of the use of medications. Pharmacists need to commit to and implement this and other innovative strategies that will increase the scope, quality, and understanding of our communication with patients that is necessary to improve compliance.

Is there a solution?

Problems of noncompliance have been recognized for more than 50 years. I could publish my 1974 paper today and not have to change three-quarters of the comments and recommendations it includes. I commend the progressive strategies that some have developed but they have not been adopted to an extent sufficient to have a meaningful impact. Studies and statistics suggest that there continues to be a high rate of noncompliance, and some contend that the problem has worsened.

Fortunately, there is a solution. Pharmacists are strategically positioned to counsel patients regarding their medications at the time they are dispensed, to contact prescribers as appropriate, and to follow up with patients to monitor their use of medications. If we don't do this, others (e.g., nurse practitioners) will. Initially, we, as individuals and as a profession, will need to assume the cost of the additional time that will be needed to implement these initiatives. Concurrently our pharmacy associations, in collaboration with independent research organizations, must conduct studies that will document the value of this extended responsibility for pharmacists, and the resultant patient benefits and reduction of costs to manage the consequences of noncompliance. Pharmaceutical companies should be requested to provide substantial grants to support this level of pharmacist involvement that will result in the more effective and safer use of their medications.

Pharmacists are the solution for noncompliance! We must take these steps now, and we will make a difference for the benefit of our patients and in the advancement of our profession!

Daniel A. Hussar

Author/Editor - Daniel A. Hussar, Ph.D.
Philadelphia College of Pharmacy, University of the Sciences in Philadelphia
Publisher - G. Patrick Polli III
Publications Director - Jeff Zajac

The opinions and recommendations are those of the author and do not necessarily represent those of his full-time employer or the publisher.

The Pharmacist Activist, 15 Shoemaker Rd., King of Prussia, PA 19406
610-337-1050 • Fax: 610-337-1049
E-mail: pharmacistactivist@news-line.com

NEWS-Line PUBLISHING