MSHP Pharmascript

Volume 44, Issue No. 1
First Quarter

Contents

Deadlines for Pharmascript Submissions

Submit articles for publication in the Spring Edition of Pharmascript by March 15, 2020
Submit articles for publication in the Summer Edition of Pharmascript by June 15, 2020

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2019 W. Arthur Purdum Award Acceptance Speech

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When I started thinking about this speech, I thought about some famous quotes about speeches. One is that all speeches should follow this formula: First, tell them what you're going to tell them. Second, tell them. Third, tell them what you just told them.

So here is part one of my speech:

First, I'm going to tell you a few interesting things that have happened in pharmacy over the last 40 years that illustrate how far we've come in that time, and some then versus now comparisons. Second, I'm going to try and tell you why I think this is such a great time to be a pharmacist.

Here is what I hope are some interesting things and comparisons of pharmacy over time:
I got my BS in Pharmacy in 1978. When I tell students that, sometimes they gasp. Sometimes they ask me what events were happening in the world back then. Were we at war with Korea then? Vietnam? It gives me a chance to talk a little history as we walk down the hall.

I went back and looked at some articles in AJHP from that year. Here are the titles of some articles I found:

- "There is a Need for an ASHP Official Position on Pharmacy Degrees, BS or PharmD"
- "Using Pharmacokinetics in Drug Therapy Management" – a relatively new thing back then
- "Using a Computerized System for Unit Dose Drug Distribution"
- "Starting a Centralized IV Admixture Service"

All things we don't think about in US hospitals today.

There are a lot of things we talked about then that we still talk about today. Here's an article titled:

- "Computerized Drug-drug Interaction Screening System – a Screen or a Sieve?" It says computerized drug interaction screening may cause too many false positives. They hadn't come up with the term "alert fatigue" yet, but this sounds like the granddaddy of that phenomenon. Interesting note - the drug interaction screening was run as a batch program once a day.
- In 1978 there were articles published about burnout (although they didn't call it that) and sterile product aseptic technique and quality assurance. Still hot topics today.

Here's a few amazing developments in Pharmacy over the last 40 years or so:

- How about the alpha receptor? I bring this up because when I was in school, one of my professors was trying to find the second alpha receptor. Now we know there are seven (four alpha-1 and three alpha-2 receptors) and they are in different locations in the body, so researchers can work on developing drugs to stimulate each one. Very cool!
- Another amazing development in pharmacy is the bar code**.** Studies of prescription filling have determined that a human filling a prescription has an error rate of 1.7%. Call it 2%, or 2 out of 100 prescriptions have an error. Of those 2%, 6.5% are clinically significant. In comparison, even the simplest barcode that might be used to fill your prescription has an error rate of 1 in 394,000 scans. That's a 0.0003% error rate and QR codes, those square things you scan with your phone and they pull up a website, they have an error rate of 1 error per 10.5 million scans!
- The smart pump – for our non-pharmacist friends, this is an IV pump combined with a computer, which will tell the nurse setting the pump whenever the infusion rate is set too high. When we first got smart pumps at Carroll around 2004, I remember looking at the data and thinking, how did patients live without these? There were so many 100 mL/hr rates that the smart pump software stopped from becoming 1000 mL/hr or 8 mL/hr that were stopped from becoming 88 mL/hr. Smart pumps are one of the biggest safety technologies of the 21st century.

I could go on with all of the stories about how we used to make chemotherapy without gloves and drip it all over the place, or how we turned the hood on to make an IV then turned it off, or pharmacists that would leave a cigarette burning in an ashtray outside the IV hood. Just ask any "mature" hospital pharmacist like me and they can tell you all those stories.

Now here is the part of the speech about why it's such a great time to be a pharmacist:

How about the job market for pharmacists?

You hear a lot about how bad the job market is for pharmacists coming out of school compared to 5 or 10 years ago. This is a quote from an APhA publication: "It's not an easy time to be a pharmacist. Across the country, pharmacists are facing layoffs, reduced hours, and harsh work conditions. Are there too many pharmacists? Is a career as a community pharmacist still viable? How can pharmacists survive and thrive in a job market in flux?"

The US Bureau of Labor Statistics (BLS) states: "Positions in traditional retail settings like grocery stores are predicted to decline in the face of increasing mail order and online pharmacy sales". The BLS also predicts that between now and 2026, an aging baby-boom generation and higher rates of chronic disease, such as diabetes, will increase demand for prescription medications, which is projected to increase demands for pharmacists in some healthcare settings.

Anyone know what happened on January 1, 2010? The "first baby boomer" turned 65. At that time there were about 78 million baby boomers (which are people born between 1946 and 1964). In 2010 when that first baby boomer turned 65, they calculated that baby boomers will start turning 65 at a rate of almost 8,000 per day, a process that will continue through the year 2039. Those people are going to need pharmacists! And pharmacy technicians!

So it sounds like the job market is going to get better.

What about pay?

In 2018, the median annual salary for pharmacists, according to the Bureau of Labor Statistics, was $126,120 annually. The lowest 10 percent earned less than $87,420 and the top 10 percent earned more than $159,410. The ranges, of course, depend largely on factors like what state you are in, rural versus urban setting, years of experience, level of education, and other variables. California, for example, has the highest paying ranges, but that's due to the higher cost of living there. In terms of hourly pay, the median pay was $60.24 per hour. That means pharmacists working for 40 years may have seen their salaries go up 8 to 10 times. How many professions can claim that?

Sadly, pharmacy technician pay has not kept pace with their increasing responsibilities; I hope this improves soon.

More good news in a then-and-now comparison:

Here are some advertisements for pharmacist jobs, by title, from AJHP in 1978:

- Clinical pharmacist; staff pharmacist position; pharmacist; director of pharmacists; faculty positions. That was about it.
- How about doing a residency? There were 86 accredited residency programs in 1978. Now there are about 3500 PGY1 positions, although I know there are more applicants than positions.

Present - Here are some job advertisements from ASHP's CareerPharm job section from this past Sunday:
We still have all those positions I just mentioned above, but today we also have:

- Applied Clinical Pharmacogenomics faculty member
- Clinical Pharmacy Specialist in Pediatric Infectious Diseases
- Clinical Pharmacotherapy Specialist in Adult Transplant Services
- Pharmacy Automation Specialist
- How about Telepharm Pharmacist? The description says, "the pharmacist will perform a medication review at the time of the call and do a complete clinical review and address any medication related questions."

That's a nice variety of job options that didn't exist before!

Here's more about what a great time it is to be a pharmacist:

Have you ever seen the video "Did You Know"? It is very interesting if you haven't seen it. It is about 6 minutes long and worth a look on YouTube. It is about the exponential increase in data over time. Here's a quote from that video: "The amount of technical data in the world is doubling every two years. That means, for students entering a 4-year technical or college degree, half of what they learn in their freshman year will be outdated by the end of their junior year."

We will need pharmacists and pharmacy technicians to handle this onslaught of new information!

Next is what I call "miracles" that pharmacists are now a part of and will be a part of in the future:

- Hepatitis C cures – When I was in school, they were trying to identify the virus. They called it "non-A / non-B" hepatitis. Now we have a cure for it!
- Monthly self-injections for migraine prevention, such as erenumab-aooe (Aimovig®).
- What do you think about a one dose treatment for depression? Brexanolone (Zulresso®) is a onetime 60-hour infusion treatment for post-partum depression.
- What's one of the biggest challenges we face in medication management? Medication non-adherence. Patients that do not take their medicines as prescribed. Medication non-adherence rates are estimated to be between 30 and 60%, with the higher rates for conditions with no symptoms, like high blood pressure. Here's an article from the lay press on that topic.
    - It's called "The Smart Pill"
      A tiny ingestible sensor which costs less than a penny is placed in a capsule or in a tablet. It gets activated by stomach juices when it's ingested. A digital signal is then sent to a Band-Aid®–sized monitor worn on the patient's arm." The sensor records when the medication is ingested, as well as the patient's heart rate, body temperature, position, rest, and activity patterns. The researcher stated: "if someone is taking a heart medicine that you want to decrease their heart rate, you can tell whether the rate is slower because the medication is working, or because the patient is inactive. The data are wirelessly transmitted to a smartphone app, which then sends it to a provider. Patients receive text message reminders if they don't take their pills."

Pharmacy is getting safer as well. We now have a strengthened USP <797> protecting patients from contaminated injectable drugs, and we have USP <800> protecting healthcare workers from hazardous drugs. People are amazed when we tell them we used to make chemotherapy drugs in a horizontal hood with no gloves and with the air blowing in our face. It will be that way one day with USP <800>. People won't believe we did not have laws and equipment protecting us from hazardous drugs. Some hospitals now have chemotherapy-making robots. More and more pharmacists and technicians will have a choice in the future whether to work in a hospital where they will have to handle chemotherapy, or where robots handle the chemotherapy. All else being equal, that would be an easy choice for me.

Pharmacy's worth is being proven over and over in terms of better patient care and cost saving. Pressure to reduce readmission has hospital administrators turning to pharmacy to help with this critical Medicare indicator. Major pharmacy organizations are lobbying for changes to the Social Security Act to allow pharmacists to be included as providers in Medicare Part B and therefore able to bill directly for outpatient services. All good things for our profession!

There are more and more sites and venues for pharmacists to work. At Carroll we just started to have a pharmacist go to doctors' offices to see patients right after the doctor does. Are you a pharmacist that wants to work at home? You can join a company that provides remote order verification done from your home or from a regional call center for hospitals

all over the country. Other roles for pharmacists include pharmacists doing and billing for wellness visits. Aside from the new job advertisements I mentioned before, I looked through GlassDoor the other day and saw jobs for: Specialty Drug Pharmacist, Compounding Center Pharmacist, Sterile Product Pharmacist, and Pharmaceutical Industry Pharmacist. The career opportunities in our profession are expanding!

In conclusion, every year for the past 5 years or so I've been invited to a career night program at University of Maryland School of Pharmacy. They have about ten tables set up with pharmacists representing various segments of institutional pharmacy. I am the community hospital pharmacy table. Each pharmacist gets a group of students for about 8 minutes and then they rotate to the next table, so we get to talk to all of them and they get to talk to all of us. In recent years the students have told me they hear it's tough to get a job, and you must have a residency to get a job in a hospital. The students try very hard to distinguish themselves from their peer group by doing volunteer work, taking on leadership roles, and doing other things. I tell them it's a great time to be a pharmacist. Yes, it is harder to get a job now than it was 10 years ago, but there are more types and more rewarding jobs available. The job market is going to improve, and pay has gone down a little in some segments and regions of pharmacy, but it's still very good. I think this little pep talk cheers them up a little.

So that was my speech. I just told you some history, some then-and-now comparisons, and finally why it is such a great time to be a pharmacist.

To close, I want to thank certain people that have made me a better pharmacist and a better person, and I wouldn't be standing up here without them.

First of all, my wife and best friend Shirley, who makes everything I do easier and better. The incredible team at Carroll Hospital, the finest team I have ever worked with. They make hard things easy and impossible things possible. Bill Lee, Tim Wu, Tricia Kokoski, Shauna Bere, and a lot of others. I'd like to thank Lisa Polinsky, our Corporate Pharmacy Director at Lifebridge, for being a kind and patient teacher and a role model for me. Thank you to Bonnie Pitt at Valley Health in Virginia, for pounding some knowledge and sense into me in the late 20th century. My first role model and still my advisor. Several people from University of Maryland, who taught me so much and gave me opportunities to grow. There are lots of other people that have helped me and my staff and shared their work with me. I am grateful to all of you. Thank you.

The Clinical Pharmacy Technician: A Novel Approach to Improving Medication Adherence and Refill Renewal Response Times

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A delay in care is when a patient does not get a medication, or any therapy that has been ordered for them in an appropriate time. A delay in treatment can lead to non-adherence, an avoidable medication management problem. Adherence is very important to improving patient outcomes, especially as it pertains to patients living with infectious diseases like Human Immunodeficiency Virus (HIV). Delays in therapy can become missed opportunities for health care if not addressed.

One approach to decreasing delays in care is by improving provider to provider communication, as many delays can be attributed to lapses in communication between the patient's care team. Patients rely on the ability of clinicians and providers, including pharmacy staff, to effectively communicate. The implementation of a clinical pharmacy technician focused on reducing delays in care, improving continuity of care, and increasing medication adherence is not only necessary, but beneficial to positive patient health outcomes.

The goal of the clinical pharmacy technician at the Bartlett Specialty Pharmacy within the Johns Hopkins Hospital is to triage prescription renewal requests by assessing the patient's past and future appointments and relevant labs. This is completed daily by utilizing the pharmacy software system and the patient's electronic health record. The clinical pharmacy technician leverages these systems to improve the turnaround time for maintenance and urgent prescription renewal requests. The clinical pharmacy technician also leads the Refill Assist Program (RAP), which is a program that aims to improve medication adherence for enrolled patients. Patients living with HIV and other infectious diseases often have social determinants that negatively impact medication adherence. The RAP provides patients prescription refill reminder calls, assistance with setting up medication delivery, communication to providers and social workers regarding lapses in insurance or non-adherence, and optional enrollment in auto-fill.

Since I have been the clinical pharmacy technician at Bartlett Specialty Pharmacy, there has been a decrease in duplicate refill renewal requests, an improvement in turnaround time for pending refill requests, and a decrease in manual faxed prescription requests sent to the Bartlett Clinic from our pharmacy. As lead of RAP, my team and I have increased patient enrollment, improved the medication possession ratio (MPR), and increased overall medication adherence for patients enrolled in the program. RAP first started two years ago as a pilot with 150 patients. Since the pilot phase, my team and I have increased patient enrollment to 400. The most recent analysis of patients from the pilot phase demonstrated a 29.5 % improvement in MPR. Additionally, medication adherence in these patients increased from 28.2% pre-enrollment to 71.8% post-enrollment. I am passionate about patient-centered care and the quality of care my patients receive. My experience as the clinical pharmacy technician has been a great learning experience. I have been able to learn more about HIV, reduce barriers to medication adherence, improve refill renewal response times, and build relationships with clinic staff and patients.

Overall, the clinical pharmacy technician is essential to enhancing and linking pharmacy services provided to patients and providers, playing a vital role in improving patient, pharmacy, and provider relationships. Through engagement of both the pharmacy staff and providers, the clinical pharmacy technician can relay information that may not be visibly understood on either end, ultimately decreasing delays in care and improving provider relationships.

Another Tragic Medication Error Involving a Neuromuscular Blocker - What Can We Learn?

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What Happened

In 2017, a registered nurse at an academic medical center in Nashville, Tennessee unknowingly administered a fatal drug to an elderly patient who was soon to undergo a full body scan.[1] The nurse was on her way to care for a patient in the Emergency Department when she was redirected to see a patient in radiology.[2] When the nurse reached radiology, she was asked to administer IV Versed® (midazolam) to help relax and control the patient's claustrophobia before a procedure. The nurse was unable to locate the medication under the patient's medication profile in the automatic medication dispensing cabinet (ADC); therefore, she used the override function and mistakenly selected and removed IV vecuronium. Vecuronium is a neuromuscular blocking agent (NMB) used to help facilitate mechanical ventilation and can cause respiratory depression if used incorrectly or in an individual for which the medication was not intended.[3] The nurse was unaware of the incorrect selection and reconstituted the powder to the concentration listed on the label. Notably, IV Versed® is available as a solution and is no longer available as a brand of midazolam. She then administered the IV vecuronium to the patient believing it was the ordered IV Versed®. The patient remained in the scanning room without monitoring, suffered respiratory depression, and died.

As a result of the unexpected patient outcome, an investigation was launched. The investigation uncovered that the nurse entered the first two letters of the intended drug ("VE") when removing the drug from the ADC, and vecuronium displayed. The ADC defaulted to generic drug name searches.[2] As a result of the nurse using the override function, a warning appeared on the screen, which contained a bolded warning stating that the medication was a paralyzing agent; however, the warning went unnoticed by the nurse.

Prevention Tips

As a result of this error, health systems should self-assess their medication use process for NMB agents. A multidisciplinary discussion of this error and a risk analysis for reoccurrence at the institution should take place. Review of the ISMP Best Practices, as well as ASHP Guidelines on the Safe Use of Automated Dispensing Devices, can aid the conversation.

According to the ISMP Best Practice 7, if NMBs are stored in ADCs, the storage practices should be standardized by keeping them in lock-lidded pockets. Additionally, ISMP recommends placement of auxiliary labels on all storage bins, ADC pockets, and drawers that contain NMBs, as well as all final medication containers that state, "Warning: Paralyzing Agent - Causes Respiratory Arrest - Patient Must Be Ventilated." Furthermore, access to NMBs should be limited to settings where mechanical ventilation support is available.

When removing medications from ADCs, name searches should require the input of the first four letters of the needed medication. The use of interactive warnings should be considered for high-risk medications stored in ADCs. In this case, an alert stating that that patient must be ventilated with a requirement that the nurse verify the information may have prompted the nurse to re-consider the appropriateness of this medication.

The use of barcode scanning prior to administration may have also identified the medication mix-up. While barcode scanning is often performed at the bedside, this type of scanning is much less frequently used in procedural areas, like radiology. Implementation of scanning technology in all areas where medications are administered should be strongly considered. Additionally, the practice for monitoring benzodiazepines should be understood. In this case, the nurse believed she administered midazolam; however, the patient was left unattended for a period of time.

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Measures of Adherence in Patients Taking Oral Chemotherapy

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"Medications don't work in patients who don't take them." - Former Surgeon General, C. Everett Koop

Treatment of cancer has historical roots as primarily intravenous administration. However, the past two decades have transformed the landscape of treating cancer, which now includes oral antineoplastic therapies as the primary treatment modality for various types of cancer.[1] Chemotherapy given via the intravenous route, is often not preferred by patients who appreciate the convenience in self-administration of oral medications at home compared to the travel and chair time involved with the more invasive administration of injectable medications at an infusion center.[2-3] However, a known downside to oral chemotherapy is the patient responsibility for adherence to a potentially complex

medication regimen that comes with varying side effects and tolerability issues.[1] The World Health Organization defines adherence as "the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider."[2] However, there is no standard definition for adherence. Nonadherence to oral chemotherapeutic regimens is a significant challenge, and may create loss of efficacy, disease progression, and increased healthcare costs.[1]

Measuring patient adherence can be done in various manners, including direct and indirect methods. Direct methods are often impractical, as they relate to directly observing the patient taking the medication, but can also include drug assays of serum or urine. Administration of oral antineoplastic agents occurs most often in the home, and not every patient who takes these medications can be monitored by these means. Drug assays are limited by medication, as many of these oral agents do not have markers that can be targeted. Indirect methods are more common, and imply that the medication has been taken by the patient.[4] These include methods such as: questionnaires, pill counts, electronic technologies, and prescription claim data. Indirect methods of measuring adherence all have their limitations since we cannot confirm the patient actually took their medications as prescribed.

Factors contributing to nonadherence are numerous, complex, and dependent on individual patients. Some potential barriers to adherence of oral chemotherapies include social, economic, system-related, therapy-related, and patient-related.[3] Therapy-related factors encompass the complexity of the medication regimen, side effects and cost, which can all affect patients in different ways. Treatment-emergent adverse effects can be a deterring factor for many patients, especially if the adverse effects are perceived as unmanageable. Patients may neglect to report adverse effects to clinicians or simply stop taking their medication.[5] Patient-related factors, including health beliefs, health literacy, and perceptions of disease and medications, can also affect a patient's adherence to oral chemotherapy regimens. System-related factors, including the relationship between patient and physician, play an important role in overall adherence and recognition of importance of therapy. Education, given by the pharmacist or other care team members, is critical to the patient's knowledge about their disease state and the treatment plan successfully translating to adherence to the plan.[4] Though often difficult, identifying a patient's barriers to adherence is a step forward in addressing nonadherence and optimizing overall care. A variety of tools have been used to measure adherence in oral chemotherapy regimens; however, there is no gold standard established for how best to measure adherence. This article will look at the different tools used to measure adherence in oral chemotherapy regimens.

Patient Reported Adherence

Oral tyrosine kinase inhibitors (TKIs) are the cornerstone of therapy for chronic myeloid leukemia (CML). Successful treatment outcomes with oral TKIs are heavily dependent on the patient's commitment to therapy and ability to adhere to a medication regimen, which can be complex due to factors such as more than once daily dosing, on-and-off cycling, or by the use of more than one medication.[5] Nonadherence to oral TKI therapy in patients with CML has been reported in approximately 22% to 41% of patients.[6] One frequently used measurement of adherence for oral TKIs is the Morisky Medication Adherence Scale (MMAS-8), an 8-item scaled tool which addresses adherence concerns such as forgetting to take medication or stopping medication without prescriber's approval. Lower scores (<6) were correlated with poor adherence, whereas a score of 8 designated high adherence.[6] Unnikrishnan et al. studied medication non-adherence in patients aged 18-65 years with CML on long term imatinib, and used the MMAS-8 as a way to measure adherence. They categorized patients with a score of 8 as 'adherent' and patients with a score ≤7 as 'non-adherent.' The median score on the 8-point MMAS-8 was 7, and 45% of patients had a score of 8 and were considered adherent to therapy.[6] Of the non-adherent patients (n=122), 48 (39%) had a score <6 , indicating low adherence.[6] Unnikrishnan et al. also used a formal quality of life (QoL) assessment that has been validated in patients with CML. After assessing the scores from the QoL assessments and MMAS-8 scales, the authors found a direct correlation between nonadherence in patients and higher symptom burden. They ultimately found that QoL was "the single most important determinant of adherence" in their study population.[6]

In addition, a study by Rychter et al. used a different questionnaire to measure adherence consisting of 17 closed questions to which patients replied at their follow-up appointments.[7] These questions included number of doses skipped, why doses were skipped, and the patient's own assessment of their adherence to treatment. Of the 140 patients who responded to the questionnaires, 72 patients (51.4%) reported skipping doses throughout their TKI treatment. Interestingly, the authors found that there was no significant correlation between adverse effects from TKIs and patients skipping or missing doses of medication. Of the 72 participants who missed doses during therapy, 38 (52.8%) of them did so due to unintentional instances such as forgetfulness.[7] The patient's self-assessment of their TKI treatment adherence showed that even non-adherent patients stated they 'always' followed instructions for their medications. This study found that a significant proportion of patients were non-adherent to their oral TKI regimen and many overestimated their adherence stating that even though they missed doses per the questionnaire, the patients also chose that they 'always' followed their regimen as prescribed.[7]

Adherence to oral chemotherapy regimens is important and influences response to therapy and disease control. However, there are few validated adherence measurement tools that can be used effectively in patients with cancer. In other disease states there are a multitude of validated measures to assess adherence, one example being in the HIV population. Wilson et al. looked at the validation of a three-item self-report measure to assess adherence in patients taking an HIV antiretroviral medication and at least one other non-HIV related chronic medication.[8] The three questions addressed the number of days that the patient took their medication, the frequency by which the medication was taken, and the patients' own rating of their adherence. Question 1 asked how many days the patient missed at least one dose of medication as a fill-in-the-blank question. The second and third questions were scaled. Question 2 asked, "how often did you take your [medication] in the way you were supposed to?" with answer choices ranging from never to always. The last question on the self-report asked, "how good a job did you do at taking your [medication] in the way you were supposed to?" These answer choices ranged from very poor to excellent. The authors found that these self-reports showed validity when compared to electronic drug monitoring (EDM) measures.[8] This self-report measurement of adherence is a simple and effective tool that could potentially be implemented in the future for patients taking oral chemotherapeutic agents.

Electronic Monitoring

Use of technology driven methods to assess adherence have become more common with the digital age, including the microelectronic monitoring system (MEMS). This system utilizes a tablet bottle that electronically records the time and date each time the cap was removed.[9] The data is then stored in an electronic system in which it generates lists and graphs that inform the person how many doses were taken and if missed or extra doses were taken. There are issues with this method of assessing adherence as well, first being the Hawthorne effect. Patients' awareness of the use of the MEMS may influence adherence. The system also comes with the issue of cost. The major limitation to this method of assessing adherence is that the act of opening a prescription bottle may not always translate to ingestion of the medication as prescribed.[9]

Medication nonadherence is one of the main factors for determining response to treatment. Ibrahim et al. presented data from a follow-up study that looked at the relationship between adherence to a TKI and the probability of losing a complete cytogenic response (CCyR) and of treatment failure in patients receiving long-term therapy.[10] Adherence, in the previous study, was measured over a 3-month period using MEMS in 87 patients receiving imatinib for a median of 59.7 months before enrollment.[11] Patients were followed after this period for a median time of 19 months, and CCyR was defined as the absence of any cells containing the Philadelphia chromosome in the bone marrow. There were 23 patients that had an adherence rate less than or equal to 90% and 18 less than or equal to 85%. During the follow-up period, 7 of those patients lost CCyR and 12 patients discontinued imatinib therapy due to various reasons. The authors found that those patients with an adherence rate less than or equal to 85% had an increased likelihood of losing CCyR at 2 years (26.8% vs 1.5%, p=0.0002). They also showed that these less adherent patients had a lower probability of remaining on imatinib compared to the more adherent patients (64.5% vs 90.6%, p=0.006).[10] From this study, the

authors showed that poor adherence is a definite influencer of treatment failure in patients with CML.

Medication Possession Ratio

Similar to treatment of CML, adherence to endocrine therapy (i.e., tamoxifen) for the treatment of breast cancer is directly related to clinical outcomes.[12] The report of the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-14 adjuvant trial for patients with early-stage breast cancer looked at adherence in this population. They found that 82% of patients taking tamoxifen were adherent at month 2 of therapy, and 72% were adherent at month 4.[12-13] The most common reason for discontinuation among these patients were adverse effects consisting of hot flashes, nausea, and vomiting. In other studies of adherence to tamoxifen for breast cancer therapy, interviews are conducted and used to assess adherence. Partridge et al. used data from prescription refill databases to evaluate adherence in this patient population. Adherence was measured as the mean percentage of eligible days in the study year in which patients had filled prescriptions for tamoxifen, also known as medication possession ratio (MPR), and this was found to be 87% in the first year of therapy.[14] There are limitations to MPR, since a paid claim for a prescription through insurance does not equate to a patient taking the medication as prescribed. Paid prescription claims may make the patient look adherent, especially if they are filling their prescription on a monthly basis but not taking the medication as prescribed.

Conclusion

Though the tools discussed in this article have been validated, there are still many barriers to effectively assessing adherence. If patients have a desire to please their physician, they may not be truthful in their responses to questionnaires administered by healthcare providers. This ultimately can lead to over-reporting of adherence in these patient populations. Patients may also refuse to fill out questionnaires, and physicians may be reluctant to continue to assess adherence in these patients. Adverse effects may also be a contributing factor to patient non-adherence, though the studies in this article found no correlation between non-adherence and medication toxicity. Overall, adherence has been shown to be a multi-faceted issue and understanding patients' needs and concerns about oral chemotherapy regimens will allow pharmacists and other healthcare providers to tackle the issue of nonadherence among patients with cancer.

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Pharmascript

Volume 44, Issue No. 1
First Quarter

New Drug Update: Lefamulin for Community-Acquired Bacterial Pneumonia

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Antibiotic resistance is a growing public health concern. Surveillance programs have observed growing trends in decreased susceptibility to current antibiotics.[1] In efforts to combat this problem, there has been a push for the incorporation of antimicrobial stewardship programs and education on public health prevention. Additionally, an expedited drug process bringing new antibiotics to the market is warranted.

Lefamulin was approved by the FDA on August 19, 2019, for the treatment of community-acquired bacterial pneumonia (CABP) in adults 18 years or older. Lefamulin is the first human systemic pleuromutilin that works by inhibiting protein synthesis at the 50S ribosomal unit. It comes in an oral and intravenous (IV) formulation. Its antimicrobial activity covers common CABP pathogens: *Streptococcus pneumoniae*, *Staphylococcus aureus* (methicillin-susceptible and possibly methicillin-resistant isolates), *Haemophilus influenzae*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydophila pneumoniae*. However, its spectrum of activity does not cover Enterobacteriaceae species or *Pseudomonas aeruginosa*. This new medication stands out amongst others because it is an effective alternative in the treatment of CABP. Lefamulin can be a great tool that addresses the issues of bacterial resistance and the adverse safety profile of fluoroquinolones.

The Lefamulin Evaluation Against Pneumonia (LEAP) Trial was composed of two trials comparing the use of moxifloxacin to lefamulin in the treatment of CABP. The primary endpoint measured the earliest clinical response time set by the FDA. Patients enrolled had a median age between 59 - 62 years old. Common comorbidities included diabetes, asthma/COPD, and hypertension.[1,2,5] Patients were selected and stratified according to their mortality risk via the Pneumonia Outcomes Research Team Risk (PORT) assessment. Trial 1 included the PORT risk classes III-V and trial 2 included risk classes II-IV. Trial 1 compared the IV lefamulin to IV moxifloxacin with the option to switch to their oral formulation after three days of IV treatment. If a patient was suspected of having MRSA, the moxifloxacin arm was given linezolid, while the lefamulin arm received a placebo pill. Trial 2 compared the oral formulation of lefamulin to moxifloxacin.[1,2]

Both trial formulations proved to be non-inferior to the standard treatment for early clinical response rate (90.8% ± 0.1% [1-sided 97.5% CI, -4.4% - Infinity]).[1] The mean duration of therapy was seven days for the IV formulation and five days for the tablets. When including multidrug-resistant *S. pneumonia*, lefamulin early clinical response rate was 100% compared to moxifloxacin at 83.3%.[1] Gastrointestinal (GI)-related events were the most common adverse events in trial 2. Diarrhea occurred in 12.2% of the lefamulin arm and 7.8% in the moxifloxacin arm.[1] However, the events were mild to moderate in severity and rarely caused the discontinuation of therapy. Of the treatment-emergent adverse events reported, 32.6% occurred with lefamulin compared to 25% with moxifloxacin.[1]

The IV formulation of lefamulin can be used safely in patients with mild to moderate hepatic impairment. In severe hepatic impairment (Child-Pugh Class C) an extension of the dosing interval to 24 hours is required.[5] The oral formulation in patients with hepatic impairment is not recommended due to limited studies. There are no renal dose adjustments required for either formulation.

Lefamulin should not be used in combination with strong to moderate CYP3A4 inducers or P-gp inducers secondary to lower AUC and Cmax. The opposite effect can be seen when using strong to moderate CYP3A4 inhibitors, CYP3A4 substrates, and P-gp inhibitors. The tablet formulation should not be used in combination with CYP3A4 substrates due to potential QT interval prolongation. Patients who are not candidates for lefamulin therapy include those with a past medical history of QT interval prolongation, ventricular arrhythmias, use of class I or III antiarrhythmic medications, or currently taking medications that could prolong QT interval.[5] If the patient must be started on lefamulin and is at risk for

QT prolongation, monitoring via electrocardiogram is required.

Patients who have a known hypersensitivity to lefamulin or any other member of the pleuromutilin class should not initiate therapy. Animal studies have shown that lefamulin can cross into the placenta and breast milk. Women who are of childbearing age should use effective barrier methods or oral contraceptives if starting this antibiotic.[5] Lefamulin is not safe to use in pregnant women. Mothers that are breastfeeding are advised to discard all breast milk while on therapy and restart feeding two days after completing therapy.[5] The most common adverse effects reported with the IV formulation are administration site reactions (7%), hepatic enzyme elevation (3%), nausea (3%), and hypokalemia (3%).[1,5] Side effects associated with the tablet formulation include diarrhea (12%), nausea (5%), vomiting (3%), and elevated hepatic enzyme elevation (2%).[1,5] Patients who develop diarrhea should be monitored for *Clostridium difficile*-associated diarrhea.[5]

The lefamulin 150 mg/15 mL 0.9% NaCl intravenous vial comes with a 250 mL citrate buffer diluent, both of which require refrigeration. Appropriate treatment is 150 mg every twelve hours by intravenous infusion over 60 minutes for five to seven days. The 600 mg tablet is to be given every twelve hours for five days on an empty stomach with a glass of water. If there is concern for GI tolerance, the tablet can be taken either one hour before a meal or two hours after. lefamulin is expensive compared to other traditional therapies. A 400 mg moxifloxacin tablet average whole sale price per treatment day can range from $9.26 – $27.23, while lefamulin has a predicted wholesale acquisition price of $205 per IV treatment day and $275 per oral treatment day.[3,4] Given its unique mechanism of action and efficacy demonstrated in phase III trials, lefamulin is an interesting alternative agent for community-acquired pneumonia. However, use of this agent for community-acquired pneumonia will be limited to third- or fourth-line therapy given the exorbitant cost, drug-drug interaction concerns, and lack of comparator studies with beta-lactam and macrolide antibiotics.

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