

Facilitating Pulmonary Arterial Hypertension Medication Adherence: Patient-centered Management



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Medication adherence is an important aspect of chronic disease management. Patient-centered management of pulmonary arterial hypertension (PAH) involves health care providers and patients discussing treatment options and agreeing on a plan of therapy. Adherence refers to the accuracy with which the patient decides to follow the chosen therapy plan, including taking medications.¹ Where compliance implies passive following of instructions, adherence is equated to active decision making and collaboration between the patient and multidisciplinary health care team.

Health care providers and patients create patient-specific interventions by establishing relationships of trust and sharing information. Self-management improves self-efficacy, which has demonstrated benefit in chronic illness management.² Self-management requires patients with PAH to be educated on all aspects of disease management. Gaining knowledge regarding basic PAH pathophysiology, historical outcomes of untreated disease progression, and current treatment options is essential for patients to understand the importance of therapy and anticipated outcomes. Medication counseling includes discussion about medication effect, dose and time interval, side effects, adverse effects, self-management, and response to skipped doses.³

Nonadherence

Medication adherence rates vary depending on particular studies but are often quoted around 50%.^{4,5} Health care providers must actively assess medication administration patterns to determine the degree of medication adherence. Deviations from prescribed therapy include not filling prescriptions, skipping doses, taking medications at incorrect intervals (early or late), or interrupting therapy. Not taking a medication course for the intended duration is a type of nonadherence common with antibiotic therapy. Dose errors, taking more or less than a prescribed dose, are another type of nonadherence. Finally, taking medications not prescribed, such as borrowing from a spouse's prescription, is another nonadherence behavior that may not be detected by providers or disclosed by patients.

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Renal transplant patients reported memory lapses and side effects as reasons for nonadherence; while health beliefs, fear of renal failure, and loyalty to the health care team and donor led to adherence.⁶ Many medication adherence studies in patients with cardiovascular and pulmonary disease have shown that patients taking complex medication regimens have lower adherence than patients taking daily medication.^{7,8} However, one study of heart failure patients demonstrated improved adherence with complex medical regimens, which was thought to be related to a higher level of attention to routine and lifestyle monitoring.⁹

Studies of adherence utilize objective and subjective measurements of individual adherence. Objective measures include pill counts, timing of refill requests, blood drug levels, and electronic monitoring devices.¹⁰ Objective measures are typically more accurate and costly. Self-reported adherence and queries of family members are subjective measures which have been documented as often inaccurate due to under-reporting.⁵

Adherence Barriers

Deviations from prescribed medication regimens occur for many reasons. Patient-specific factors such as perceptions, expectations, beliefs, motivation, and knowledge affect medication adherence.⁵ Patient forgetfulness is the most commonly reported barrier.^{5,6} Knowledge deficits regarding a medication's mechanism of action, side effects, and expected benefit of treatment influence a patient's decision to follow a prescribed therapy. A patient's condition contributes to medication adherence. Severity and progression of symptoms can limit ability and motivation to complete treatments. Depression, anxiety, and cognition affect decision making and self-management.⁷ Patients with several comorbidities may have increasingly complex medical regimens and combined mental and physical factors which result in increased nonadherence.

Barriers related to the health care system must be considered. Patient and provider interactions can interfere with patient understanding of prescription directions. Effectiveness of communication and listening skills facilitate trust between the patient and the multidisciplinary team. Providers are increasingly challenged with inadequate time to discuss disease state, potential therapies, and each therapy's benefits and challenges. Providing essential information to patients improves knowledge, decision

making, and self-management.

In addition to patient and health care system barriers, environmental, social, and financial factors influence adherence to medications and necessary lifestyle changes.⁵ Burdens such as lack of social support, cost of medications, and limited transportation to the clinic or pharmacy can contribute to challenges despite desired adherence. Long-term adherence barriers may be related to an individual response to therapy, side effects, and the convenience or restrictions related to a prescribed regimen.⁷

Oral Pulmonary Arterial Hypertension Therapy

As with other chronic illnesses, challenges specific to oral PAH therapy exist. Decreased adherence has been demonstrated with dosing frequencies of 3 or more times per day.⁷ For example, patients often express difficulty remembering the middle dose of sildenafil because of work schedules or side effects. Other patients have reported noting increased symptoms after a delay of a dose of sildenafil, prompting the missed dose to be taken immediately, leading to inconsistent dosing intervals.

Diuretics prove challenging to patients who travel or are not homebound and are often self-adjusted to prevent urgency or incontinence. To maintain euvolemia, patients may be instructed to monitor daily weights and signs and symptoms of fluid retention, and then adjust diuretics and potassium as needed. Repeated changes in dose and frequency of diuretics make it difficult for patients to maintain an updated medication list and may be confusing. While some patients may be capable of self-titrating diuretics and potassium with instruction and close monitoring of kidney function and potassium levels, other patients will not report weight gain and may unsafely self-medicate without supervision of the health care team.

Medications that require monthly lab testing such as endothelin receptor antagonists or warfarin may influence adherence and drug monitoring due to inconvenience or difficulty with phlebotomy. Oral PAH therapies can be financially burdensome because of high copayments and gaps in insurance coverage. Despite patient assistance programs, time-consuming paperwork processing can result in delays of medication availability. Awaiting reimbursement approval because of mandated prior authorizations for prescription initiation and after insurance changes at times of open enrollment could result in interrupted therapy. It has been reported that a minority of patients reinstate medications that were discontinued because of inability to pay during periods of excessive copay such as pharmacy benefit caps or gaps in coverage.¹¹ Patients may be complacent when communicating with insurance companies, pharmacies, and health care providers citing lack of social support or the energy required for exploring coverage options.

Inhaled Pulmonary Arterial Hypertension Therapy

Adhering to dosing schedules where nebulized therapy is administered many times a day can be challenging. For some patients, treatment time and frequency may be difficult to incorporate into active lifestyles. One sample of patients with asthma and chronic obstructive pulmonary disease demonstrated nonadherence in 72% of refilled prescriptions. Of this total, 59% of patients were under-dispensed a prescribed preventative therapy according to insufficient refill requests.¹² Because of the frequency of inhaled prostacyclin treatments, patients have reported missed and delayed doses caused by scheduled appointments, forgetting, or losing track of time. Inhaled treatments require additional time for

drug delivery set-up, inhalation, clean-up, and packing of the device when leaving home. Because there are multiple steps to maintain continuity of inhaled therapy, interruptions and delays can occur for numerous reasons. Completing inhaled treatments in public could incite embarrassment and questions about therapy, thus making patients reluctant. Troubleshooting inhalation device alarms or problems in delivery may interfere with scheduled treatments. Side effects including lightheadedness, headache, flushing, cough, or throat irritation have been reported by patients as additional causes for missed doses.

Infused Pulmonary Arterial Hypertension Therapy

Prior to initiation of continuous infusion therapy, hands-on pump and drug reconstitution training can be helpful for patients to determine if this is a desired treatment option and for the PAH provider to assess whether the patient is capable of safely managing the therapy. Initially, symptoms of fatigue, shortness of breath, and decreased concentration caused by hypoxia or decreased perfusion may make it difficult or impossible for patients with PAH to manage infused therapy independently. Adequate social support is necessary until symptoms improve and the patient is able to function independently. In addition, during long-term therapy, patients may develop physical or cognitive barriers requiring assistance. Therefore, ongoing social support is essential to prevent drug errors and interruptions if the patient becomes incapable of maintaining therapy.

Chronic prostacyclin infusions have been interrupted, accidentally and intentionally, despite understanding of potential rebound PAH symptoms. Patients have reported neglecting to restart infusions after routine maintenance. After discovery of an extended interruption, infusions have been restarted at full dose, which may result in instability and excessive side effects. It is possible that patients may become complacent or nonadherent after being on therapy for an extended time. Therefore, safety must be reassessed frequently with patients on continuous infusion therapy. Patients at high risk for medication errors, interruptions, boluses, or improper administration technique could have life-limiting complications with infusion therapy.

Nonadherence to aseptic technique can lead to sepsis or central line site infections, requiring additional management and resources. Infusion pump therapy prompts public questioning and travel complications. For some patients, the embarrassment and inconvenience of performing activities of daily living connected to a continuous infusion have prompted interruption in infusions. Concealing therapy may be important to patients with employment or social concerns.

Side effects of PAH prostacyclin medications including headaches, nausea, diarrhea, foot or leg pain, and subcutaneous site pain are often reported as irritating and may require additional medications to tolerate prostacyclin therapy. Additional medications increase the complexity of the regimen and can cause additional side effects. Patients may be reluctant to increase the prostacyclin dose when side effects interfere with daily activity or special occasions.

Oxygen Therapy

Adherence to supplemental oxygen therapy at prescribed doses may not be feasible because of equipment limitations, inadequate portability, and inadequate reimbursement of therapy. Frequently, patients report not titrating oxygen flow with activity because they forget to increase liter flow. Attempting to conserve portable oxy-

gen related to limited quantity and fear of running out of oxygen when away from home can lead to nonadherence.

Altered body image is commonly reported related to oxygen therapy. Patients report frustration at having to explain oxygen therapy to children and a community perception that smoking is the reason for the therapy. Because patients may not identify the positive benefits of oxygen therapy in improving health and symptoms, there may be an unwillingness to adhere.¹³

Assessment of Adherence

It is necessary for PAH health care providers to understand, assess, and develop patient-specific interventions to improve medication adherence. Improved outcomes have been demonstrated with medication adherence in chronic illnesses such as heart failure, hypertension, and diabetes.^{1,14} Preventable hospitalizations for worsening PAH symptoms, heart failure exacerbations, and infections may decrease with improved PAH therapy adherence.

Assessing medication adherence is limited by inaccuracy of self-reporting when compared to costly objective measures.⁸ Adherence assessment should include measurement of the percentage of overall prescribed doses taken. In addition, comparing the percentage of days that the correct number of doses were taken with the percentage of doses that were taken on schedule are important aspects of understanding patient adherence.¹⁵ Assessing patients' confidence in taking medications as prescribed can be helpful in determining self-efficacy in some patient populations.¹⁶ Assessing confidence of adherence despite anticipated specific medication challenges and side effects can provide insight into patient motivation and expectations.

Adherence Interventions

Discussion and assessment of medication adherence should occur with every clinic evaluation. Asking patients to bring pill bottles to clinic visits can help patients and providers communicate about medications initiated or discontinued between visits and frequency of requested refills. Special attention to medication adherence should be discussed with any signs of clinical worsening as a potential, reversible cause of deterioration. Assessing the frequency of refill requests by contacting the patient's pharmacy can provide insight into ratio of intended vs taken dose days.

Utilization of pillboxes, timers, cell phone alarms, or notes can provide reminders for identified nonadherence caused by forgetting. Home health nursing may be helpful by providing an in-home assessment of adherence, frequency of missed doses, and response to patient-specific interventions. Simplification of medication regimens may be helpful. Discontinuation of nonessential medications can be assessed by PAH specialists or primary care providers.

Discussion of cultural concepts of social support or perceived burden on family dynamics can provide insight to the health care team. Consultation with social services may be needed to address social or financial factors. Assigning tasks to the family may help patients who are reluctant to ask for help. Identification of barriers to adherence and corresponding solutions can empower patients to make changes in collaboration with the PAH multidisciplinary team.

Upon therapy initiation and with identified nonadherence, patient education should include discussing what to do if doses are missed and when to skip a dose. Reminding patients of the potential harm of overdosing by early administration or increased dosage may prevent hypotension with vasodilator therapies. De-

pending on the specific PAH therapy, the importance of contacting the health care providers before restarting medications if an interruption of a specified duration occurs should be discussed. Emphasizing the importance of taking medications instead of focusing on exact dosing times can help patients understand that the schedule is not difficult or restrictive.¹⁵ Communication that is not confrontational but conveys concern for patient safety may clarify the consequences of risky behaviors. Reinforcing behavior or identifying benefits of adherence such as decreasing clinic visits, avoiding hospitalizations, or improving functional capacity can encourage positive behaviors.¹⁷

Pharmacist interventions have been shown to improve medication adherence and reduce hospitalizations and health-related costs in the heart failure patient population.¹⁸ Specialized pharmacists assess medication history, including prescribed and over-the-counter medications, then provide verbal and written instructions for simplified medication regimens. Pill bottles can be coded with a symbol that is repeated on the printed medication timeline to help identify and simplify dosing schedules. Subsequent monitoring of medication use and changes in symptoms are communicated to the clinic nurses and providers.¹⁸ Providing consistent interactions and creating relationships among specialty pharmacists and patients on PAH therapy may provide similar benefits.

Conclusion

Medication adherence is one important aspect of the lifestyle modifications necessary for patients with PAH. A major concern for negative outcomes exists when medication nonadherence is combined with the severity and progression of untreated PAH. Increased health care costs from inadequate treatment and cost of therapies not properly utilized in this patient population creates further burden in the health care system. Open communication regarding patient perceptions of medication use and adverse effects must be ongoing to help providers identify patients at high risk of nonadherence.¹⁹ Assessment of barriers to adherence must include not only patient and provider factors, but cultural, social, and financial barriers as well. When nonadherence is identified, individualized interventions to improve PAH therapy adherence are necessary.

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