Case Series

Open Access

CrossMark

Use of a digital medicine offering in hypertension management: a case series

Abstract

Hypertension is a common, modifiable risk factor for premature morbidity and mortality. While medication nonadherence has been shown to be a major cause for poorly controlled hypertension, it can be difficult to distinguish medication nonadherence from suboptimal therapy. We describe the use of digital medicines in 3 patients with uncontrolled hypertension. This report illustrates how objective medication ingestion adherence data obtained through the use of a digital medicine offering can improve the effectiveness of hypertension management.

Keywords: adherence, hypertension, chronic care management, digital medicines

Naunihal S Virdi, Jose R Criado
Proteus Digital Health, USA

Correspondence: Naunihal S Virdi, Proteus Digital Health, Inc. 2600 Bridge Parkway, Redwood City, California, USA, Tel 6506376207, Email nvirdi@proteus.com

Introduction

Hypertension is both a common and dangerous chronic health condition affecting a third of adults in the United States.[1] Uncontrolled blood pressure (BP) is a major risk factor for myocardial infarction, stroke, congestive heart failure, and renal failure.[2] While medication nonadherence is known to be a major cause for poorly controlled hypertension,[3] its assessment in clinical practice and distinguishing it from inadequate medication dosing can be difficult.[4] Consequently, there remains an unmet need for clinicians to objectively determine the medication-taking behavior of their patients with uncontrolled BP in order to make more accurate medical treatment decisions.

Proteus Discover™ was developed precisely to address this need. This digital medicine offering (DMO) consists of digital medicines (medicines co-encapsulated with an ingestible sensor, which upon ingestion transmits a signal), wearable sensor patch (detects the ingestible sensor signals to measure medication adherence; also measures physical activity and rest duration, step count, and heart rate), patient mobile app (to visualize the DMO data), and provider web portal (summarizes DMO data). The technology has been FDA cleared.

We describe 3 cases of uncontrolled hypertension (systolic blood pressure ≥140mmHg) in patients who also have uncontrolled type 2 diabetes(A1C≥7%) who used the DMO for 4weeks as part of an IRB approved, 12week, cluster-randomized, clinical study. In this study patient using the DMO had greater reductions in blood pressure, glycated hemoglobin, and low density lipoprotein cholesterol than patients receiving usual clinical care.[5,6] All subjects had failed their current therapy, consisting of stable doses of at least 2 antihypertensives (≥30days at the same doses) and metformin and/ or sulfonylurea (≥90 days at the same doses of metformin and/or sulfonylurea). Subjects using the DMO were switched to digital forms of their medications to allow for ingestion adherence measurement. The antihypertensive regimen and doses were left unchanged initially to allow the provider to gain insights about the blood pressure response when the patient's ingestion adherence was also being measured. This case series illustrates how this DMO can help clinicians determine the appropriate next steps in hypertension management for their patients.

Case series

Patient 1: Needs medication titration

The first patient is a 60year-old, Hispanic white male, employed, with a college education who uses a mobile device daily. He was diagnosed with hypertension and diabetes in 2006. His baseline BP was 165/87mm Hg. The patient used the DMO along with digital hydrochlorothiazide (HCTZ 25mg once daily) and lisinopril (40mg once daily) for hypertension.

Two weeks after starting the DMO, his BP remained elevated (157/85mm Hg). Ingestion adherence per medicine was 100% for HCTZ and lisinopril. During the initial two weeks his average daily step count was 6718 steps per day. As the patient's BP was still too high while adherent, the provider knew the patient required additional antihypertensive medication. The patient was then prescribed digital amlodipine (5mg twice daily). The patient returned 4weeks after starting DMO and his BP was reduced (120/70mm Hg). Average ingestion adherence for the interim 2weeks was 96% for HCTZ and 100% for both lisinopril and amlodipine. During this time, he had an increase in his average daily step count to 7463 steps per day after receiving coaching based on DMO data. At his final study visit (12weeks after starting DMO), his BP remained under control, 129/77mm Hg.

Patient 2: Needs adherence support

This patient is a 60year-old, non-Hispanic, African American male, unemployed, with less than a high school education and who uses a mobile device daily. He was diagnosed with hypertension and type 2 diabetes, along with heart failure and peripheral neuropathy 3years prior to screening. His baseline BP was 166/105mm Hg. He was prescribed digital losartan (100mg daily). He continued to take carvedilol 25mg daily (not digitized) for hypertension.

After 2weeks on DMO, the patient's systolic BP was reduced to 132/91mm Hg. Ingestion adherence to losartan was 77%. His average daily step count was low at 1798 steps per day. Because the patient was able to achieve a BP at goal without a medication titration after achieving high adherence to his medicines, it was believed that

adherence was the root cause for the uncontrolled BP. No changes were made to the patient's medication regimen. Assessment of the patient at the next visit to the clinic 4weeks after starting the DMO showed a further reduction in both systolic and diastolic BP (112/79mm Hg). Average ingestion adherence for the 2 interim weeks for losartan was 78.6%. During the prior 2weeks, his average daily step count remained about the same at 1719. At the final visit 8weeks later, the BP remained lower than at baseline, 128/90mm Hg.

Patient 3: Medication doses too high

The final patient is a 73year-old non-Hispanic retired female who completed some college. She was diagnosed with type 2 diabetes in 1995 and hypertension in 1999. In addition, she was diagnosed with hypothyroidism and depression. Her initial BP was 169/74mm Hg. The patient was prescribed digital HCTZ (25mg once daily) and losartan (100mg once daily). For hypertension, the patient was also taking atenolol 100mg daily that was not digitized.

Assessment 2weeks after initial screening showed that her BP was reduced (127/77 mm Hg); she also complained of dizziness and some home BP values indicated that she may have been on too high a dose of BP meds. Ingestion adherence for the first two weeks for both HCTZ and losartan was 92%. During the initial two weeks her average daily step count was 2488 steps per day. The patient's HCTZ dose was then reduced to 12.5mg (once daily).

Assessment of the patient at the next visit to the clinic 2weeks later showed that BP remained low (116/76mm Hg) without dizziness symptoms. Ingestion adherence for HCTZ and losartan as well as metformin was 100%. The average daily step count remained about the same at 2596 steps per day. At her final visit 8weeks later; her BP remained low, 104/72mm Hg, without symptoms.

Discussion

Medication nonadherence is the most common reason for apparently resistant hypertension.[3] The WHO estimates that about 50% of patients are not medication adherent.[6] In addition to being common, medication nonadherence is also quite expensive, costing $290billion annually.[7] In patients who have their diabetes or hypertension well controlled, nonadherence still leads to excess hospitalizations and mortality.[8] Treatment guidelines for hypertension as well as diabetes mellitus recommend assessment of medication adherence. While ingestion adherence data obtained using digital health monitoring has been shown to support patient education and promote patient engagement in self-care,[5,6] this case series illustrates through patient examples how this DMO facilitates medication adjustments and improves clinical outcomes by providing objective ingestion adherence data to both the patient and provider.

The first two cases illustrated two different decisions that can be made after understanding if uncontrolled hypertension is related to nonadherence, inadequate medication doses, or a combination of both. The first case highlights how objective ingestion adherence data, allowed the provider to make an informed medical decision to titrate the medication dosage. The second case, in contrast, shows a case where additional medication would not have helped the patient and as illustrated in the final case, may have led to adverse outcomes.

Hypertension management in the geriatric population has been a concern due to complications and adverse side effects.[2–9] Antihypertensives have been associated with a higher risk of serious injuries due to falling in the elderly.[9,10] There is evidence that antihypertensive drugs are associated with orthostatic hypotension.[9–11] The reported prevalence rate of orthostatic hypotension is not clear; rates between 6% and ≥35% have been reported in patients with hypertension and diabetes.[11] The final case highlights this concern and the dangers of making medication adjustments in the absence of objective adherence data. In this case, the antihypertensive regimen needed to be reduced in order to promote adherence and ensure patient safety. Reducing the dose of HCTZ from 25 to 12.5mg showed that systolic BP remained low while dizziness symptoms resolved. With the DMO, the provider was able to diagnose the root cause for the uncontrolled BP accurately.

As described in the introduction, all 3 patients had failed their current antihypertensive regimen. This regimen was not changed at the start of the DMO and the patients received digital forms of the same medications. As seen in all 3 cases DMO patients usually maintain a high level of ingestion adherence while using the offering. It is hypothesized that the patients are engaged due to the feedback of actual ingestion data and the knowledge that their providers would also be able to see the data. Providers can also use this data to reinforce the cause and effect relationship between adherence and level of blood pressure control.

Conclusion

Objective ingestion adherence data may improve medical decision-making for chronic disease management. This case series illustration how timely, objective ingestion adherence data is used to make clinically meaningful treatment decisions. The DMO enables patients and providers to view actual medication ingestion adherence data, allowing them to reorient patient conversations from general inquiries about medication adherence to using objective data to address specific root causes for failing to achieve therapeutic goals or experiencing medication side-effects. The DMO also directly supports patient medication ingestion adherence. By enabling better decision making and supporting medication adherence, this DMO helps to improve clinical outcomes.

Acknowledgements

Conflict of interest

Naunihal Virdi is an employee of Proteus Digital Health, Inc. Jose Criado was a paid contractor of Proteus Digital Health, Inc.

References

1. James PA, Oparil S, Carter BL, et al. Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507–520.

2. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2013;31(7):1281–1357.

3. Tobe SW, Lewanczuk R. Resistant hypertension. *Can J Cardiol*. 2009;25(5):315–317.

4. Burnier M, Wuerzner G, Struijker-Boudier H, et al. Measuring, analysing, and managing drug adherence in resistant hypertension. *Hypertension*. 2013;62(2):218–225.

5. Frias J, Virdi N, Raja P, et al. Effectiveness of Digital Medicines to Improve Clinical Outcomes in Patients with Uncontrolled Hypertension and Type 2 Diabetes: Prospective, Open-Label, Cluster-Randomized Pilot Clinical Trial. *J Med Internet Res* 2017;19(7):e246.

6. WHO. *Adherence to Long-Term Therapies: Evidence for Action*. Switzerland; 2003. p. 1–209.

7. *Thinking outside the pillbox: a system-wide approach to improving patient medication adherence in chronic disease*. New England Healthcare Institute, USA; 2009:1–21.

8. Ho PM, Rumsfield JS, Masoudi FA, et al. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Arch Intern Med*. 2006;166(17):1836–1841.

9. Zia A, Kamaruzzaman SB, Tan MP. Blood pressure lowering therapy in older people: Does it really cause postural hypotension or falls? *Postgrad Med*. 2015;127(2):186–193.

10. Tinetti ME, Han L, Lee DS, et al. Antihypertensive Medications and Serious Fall Injuries in a Nationally Representative Sample of Older Adults. *JAMA Intern Med*. 2014;174(4):588–595.

11. Ricci F, De Caterina R, Fedorowski A. Orthostatic hypotension: Epidemiology, prognosis, and treatment. *J Am Coll Cardiol*. 2015;66(7):848–860.