Off-Label Drug Uses

Prazosin: Benign Prostatic Hyperplasia

Joyce A. Generali, RPh, MS, FASHP (Editor),* and Dennis J. Cada, PharmD, FASHP, FASCP†

This *Hospital Pharmacy* feature is extracted from *Off-Label Drug Facts*, a publication available from Wolters Kluwer Health. *Off-Label Drug Facts* is a practitioner-oriented resource for information about specific drug uses that are unapproved by the US Food and Drug Administration. This new guide to the literature enables the health care professional or clinician to quickly identify published studies on off-label uses and determine if a specific use is rational in a patient care scenario. References direct the reader to the full literature for more comprehensive information before patient care decisions are made. Direct questions or comments regarding *Off-Label Drug Uses* to jgeneral@kumc.edu.

BACKGROUND

Benign prostatic hyperplasia (BPH), one of the more common diseases in aging men, is caused by a nonmalignant proliferation of the stromal and epithelial cells in the prostate gland. Often, but not always, BPH is associated with a progressive evolution of bothersome lower urinary tract symptoms (LUTS), including urinary frequency, urgency, nocturia, decreased and/or intermittent force of urinary stream, and the sensation of incomplete bladder emptying. In addition, not all patients with BPH and LUTS will have prostate enlargement. The mainstay of therapy for mild symptoms is watchful waiting until pharmacological therapies are needed. Surgical correction is usually considered for severe cases. The drugs of choice for BPH include alpha-adrenergic blocker therapy or 5-alpha-reductase inhibitors. The utility of alpha adrenergic blockers is based on their ability to inhibit bladder outlet obstruction that is related to alpha-1 adrenergic mediated contraction of prostatic smooth muscle. In the United States, 4 alpha adrenergic blockers are US Food and Drug Administration (FDA)-approved for use in the management of BPH, of which 2 are also indicated for the management of hypertension. Prazosin, an older alpha-1 adrenergic blocker, is FDA approved for the use in hypertension only.¹

PATIENT POPULATION

Male patients with mild to moderate BPH.

DOSAGE AND DURATION

Oral doses of prazosin 0.5 mg twice daily were administered for 2 weeks, then doses were doubled for an additional 2 weeks.²

RESULTS

Prazosin in the management of BPH has had limited study compared to other alpha adrenergic blockers.² No studies have been published regarding the use of prazosin in BPH management since the American Urology Association published its BPH guidelines.¹

Guidelines

The American Urology Association Guidelines on the Management of BPH states that 4 alpha-adrenergic blockers are considered an appropriate treatment option for patients with LUTS secondary to BPH. These include alfuzosin, doxazosin, tamsulosin, and terazosin. The guidelines also state that data are insufficient to support a recommendation for use of prazosin as treatment of LUTS secondary to BPH.¹

Noncontrolled Trials

In an open randomized study, 121 male patients were randomized to receive treatment with prazosin, terazosin, or tamsulosin for 4 weeks. Initial doses were 0.5 mg of prazosin or terazosin twice daily or 0.1 mg of tamsulosin once daily for 2 weeks and then doubled for the final 2 weeks. Patients rated symptoms on a 6-point

*Editor-in-Chief, *Hospital Pharmacy*, and Director, Drug Information Center, Kansas University Medical Center, 3901 Rainbow Boulevard, Kansas City, Kansas 66160, e-mail: jgeneral@kumc.edu; †Executive Editor, *The Formulary*, and Editor, *Off-Label Drug Facts*, e-mail: Dennis.Cada@wolterskluwer.com.

scale from 0 (*absence of symptoms*) to 5 (*severe symptoms*), including nocturia, frequency, urgency, decreased force and size of urinary stream, straining, intermittency, and sensation of residual urine. A total of 16 patients were excluded from data analysis, leaving 105 patients who qualified for evaluation. Four patients (1 in the prazosin group and 3 in the terazosin group) withdrew due to adverse events. At the end of 4 weeks, there was a significant improvement in total symptom score when compared to baseline in the prazosin, terazosin, and tamsulosin groups (38%, 39%, and 26%, respectively). Terazosin demonstrated a significantly greater improvement in urgency, sense of residual urine, prolonged micturition, and intermittency than tamsulosin. Uroflowmetry results examined in 50 patients revealed that at 2 weeks no significant improvement was observed with any agent in maximal or average flow rate or residual urine (percentage voided). At 4 weeks, a significant increase in maximal flow rate (2.8 mL/s) was noted with prazosin and in average flow rate (1.3 mL/s) with tamsulosin. No significant changes were observed in residual urine ratio in any treatment group.²

SAFETY

This is a limited safety profile. Refer to package labeling for complete prescribing information (eg, warnings/precautions, adverse reactions, drug interactions).

In the reviewed data, 6 adverse events were reported in 5 patients. All events occurred within the first

2 weeks of treatment. A total of 4 patients withdrew from the study: 1 in the prazosin group due to dizziness, and 3 in the terazosin group (eg, thirsty, nausea and dizziness, asthenia). One patient in the tamsulosin group had fever that was considered not treatment related. Significant decreases in blood pressure were observed at 4 weeks in hypertensive patients with prazosin and terazosin therapy. No changes were observed in normotensive patients.²

THERAPY CONSIDERATIONS

The use of prazosin therapy in the management of BPH cannot be recommended at this time based on the limited availability of data and the availability of other effective agents in this class. The American Urology Association Guidelines on the Management of BPH state that data are insufficient to support a recommendation for use of prazosin as treatment of LUTS secondary to BPH.¹

REFERENCES

1. AUA Practice Guidelines Committee. AUA guideline on management of benign prostatic hyperplasia. Chapter 1: Diagnosis and treatment recommendations. *J Urology*. 2003; 179:530-547.
2. Tsujii T. Comparison of prazosin, terazosin and tamsulosin in the treatment of symptomatic benign prostatic hyperplasia: a short-term open, randomized multicenter study. *Int J Urol*. 2000;7:199-205. ■