Off-Label Drug Uses

Risperidone: Stuttering

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@ku.edu.

BACKGROUND

Stuttering, a condition in which the normal pattern, rhythm, or timing of speech is disrupted, may be characterized by repetition and prolongation of words, phrases, and sounds, as well as hesitations or pauses that interrupt speech flow. Causes may be developmental (occurring in childhood), neurogenic (eg, head injury, stroke), or psychogenic (related to emotional trauma or stress). Because mild stuttering is often self-limiting, it is rarely treated. Patients with more severe forms often require speech therapy and counseling. Pharmacological therapy has produced inconsistent results or has been limited by side effects.^{1,2} It has been suggested that an antidopaminergic effect may be beneficial in reversing stuttering problems.³ Risperidone, an antipsychotic approved for various psychiatric disorders, has broad neurotransmitter activity including antidopaminergic action and may be useful in resolving stuttering.

PATIENT POPULATION

Adult patients with developmental stuttering.

DOSAGE AND DURATION

Dosage range is 0.5 mg to 2 mg daily. Initial dosing may begin as 0.5 mg nightly, increased by 0.5 mg daily every 4 days or more as tolerated to a maximum of 2 mg daily.

SCALES

The Stuttering Severity Instrument for Children and Adults - Third Edition (SSI-3) is an objective measurement of overall stuttering severity via analysis of an audio/videotape of the subject speaking 200 to 500 words of standardized conversation and reading tasks randomly assigned. The assessment incorporates ratings of the percent syllables stuttered of syllables spoken, the duration of stuttering events, and the physical concomitants of stuttering behavior (eg, associated struggle, tic motions).

RESULTS

The evaluation of risperidone in the management of developmental stuttering is limited to small controlled trials and case report data, enrolling less than a total of 50 patients and demonstrating beneficial effects in several scale measurements of stuttering.

Controlled Trials

Risperidone has been studied in 2 small controlled trials for the management of developmental stuttering in adults.^{4,5} Both studies were performed by the same investigator group. In a 6-week, double-blind, placebo-controlled trial, 16 adult patients with developmental stuttering (onset prior to 6 years of age) and a minimum SSI-3 score of 15 were randomized

*Editor-in-Chief, *Hospital Pharmacy*, and Clinical Professor, Emeritus, Department of Pharmacy Practice, University of Kansas, School of Pharmacy, Kansas City/Lawrence, Kansas, e-mail: jgeneral@ku.edu; Founder and Contributing Editor, *The Formulary*, and Editor, *Off-Label Drug Facts*, e-mail: Dennis.Cada@wolterskluwer.com.

to receive either risperidone 0.5 mg nightly titrated to 2 mg nightly or placebo. When compared with baseline, there were significant improvements in the risperidone group for most scale measurements, including the mean SSI-3 score (25.3 vs 17.5; $P < .001$), the percentage of syllables stuttered (%SS; 9.6% vs 4.7%; $P < .01$), and the time spent stuttering as a percentage of total time speaking (%TS; 28% vs 16.7%; $P < .01$). The duration of stuttering was unaffected (4.5 vs 3.2 seconds). In contrast, there were no significant changes in the placebo group for the same measurements from baseline to the end of the study period.⁴ In a similar 6-week study design, 21 adults with developmental stuttering (onset prior to 6 years of age) were randomized to receive risperidone (same dose as above study) or placebo. When compared with placebo, risperidone significantly improved mean SSI-3 scores (3.93 vs 5.23; $P < 0.05$) but not the %TS (4.75% vs 4.41%).⁵

Case Reports

Two case reports described the beneficial effects associated with risperidone treatment in persistent developmental stuttering. Both adult patients (ages 42 and 24 years) experienced significant reductions in tic-like motor behaviors and linguistic dysfluencies after risperidone therapy was initiated. Dosages ranged from 0.5 mg to 2 mg daily.^{6,7}

SAFETY

This is a limited safety profile. Refer to package labeling for complete prescribing information (eg, Warnings/Precautions, Adverse Reactions, Drug Interactions).

Adverse reactions were reported in only 1 of the controlled trials.⁴ The drug was generally well tolerated without evidence of extrapyramidal symptoms. Sedation occurred in 3 patients but was transient and responded to dose reduction. Galactorrhea and amenorrhea occurred in a female patient and persisted when the dose was reduced from 1 to 0.5 mg daily. The patient completed the trial, and the symptoms reversed within 2 months of drug discontinuation. Risperidone-induced stuttering has been reported in a limited number of case reports describing adult patients receiving 4 mg daily.^{8,9}

Risperidone product labeling contains a boxed warning regarding an increased mortality in elderly patients with dementia-related psychosis.¹⁰

THERAPY CONSIDERATIONS

The use of risperidone in the management of developmental stuttering is limited to small controlled trials and case report data and demonstrates beneficial effects. This drug may be a therapeutic option in the management of stuttering in adults, but it requires further evaluation in larger controlled trials.

REFERENCES

1. Boyd A, Dworzynski K, Howell P. Pharmacological agents for developmental stuttering in children and adolescents: A systematic review. *J Clin Psychopharmacol*. 2011;31(6):740-744.
2. Ashurst JV, Wasson MN. Developmental and persistent developmental stuttering: An overview for primary care physicians. *J Am Osteopath Assoc*. 2011;111(10):576-580.
3. Brady JP, Ali Z. Alprazolam, citalopram, and clomipramine for stuttering. *J Clin Psychopharmacol*. 2000;20:287.
4. Maguire GA, Riley GD, Franklin DL, Gottschalk LA. Risperidone for the treatment of stuttering. *J Clin Psychopharmacol*. 2000;20:479-482.
5. Maguire GA, Gottschalk LA, Riley GD, Franklin DL, Bechtel RJ, Ashurst J. Stuttering: Neuropsychiatric features measured by content analysis of speech and the effect of risperidone on stuttering severity. *Compr Psychiatry*. 1999;40:308-314.
6. Ranjan S, Sawhney V, Chandra PS. Persistent developmental stuttering: Treatment with risperidone. *Aust N Z J Psychiatry*. 2006;40(2):193.
7. Tavano A, Busan P, Borelli M, Pelamatti G. Risperidone reduces tic-like motor behaviors and linguistic dysfluencies in severe persistent developmental stuttering. *J Clin Psychopharmacol*. 2011;31(1):131-134.
8. Lee HJ, Lee HS, Kim L, Lee MS, Suh KY, Kwak DI. A case of risperidone-induced stuttering. *J Clin Psychopharmacol*. 2001;21:115-116.
9. Yadav DS. Risperidone induced stuttering. *Gen Hosp Psychiatry*. 2010;32(5):559.e9-10.
10. *Risperdal* [product information]. Titusville, NJ: Ortho-McNeil-Janssen Pharmaceuticals, Inc.; 2007. ■