

Use of Cetirizine in a 23-Month-Old Male Causes Insomnia

Melissa C. Jones, PharmD, BCPS, and Curtis E. Jones, II, PhD, RPh

Abstract: Allergic rhinitis affects approximately 40% of children and generally presents in children from 10–19 years of age; however, the condition has been seen in children as young as 6 months. Antihistamines are commonly prescribed in infants and children for the relief of allergic symptoms. A 23-month-old male with a history of chronic otitis media was prescribed cetirizine 2.5 mg daily at bedtime for maintenance of his chronic rhinitis symptoms. Several days into therapy, the child began experiencing frequent and progressive nighttime periods of awakening. Once treatment was discontinued, the child resumed his normal sleeping patterns.

Key Words: cetirizine, insomnia, toddler

Antihistamines are commonly used in infants and children for the relief of allergic symptoms such as rhinorrhea, sneezing, and nasal congestion, with relatively positive outcomes. Allergic rhinitis affects approximately 40% of children and generally presents in children from 10–19 years of age¹; however, the condition has been seen in children as young as 6 months.² The condition predisposes patients to otitis media with effusion and bacterial sinus infections resulting from inflammation and obstruction of the eustachian tubes and sinuses. Therefore, antihistamines represent a logical adjunctive therapy that may mitigate episodes of otitis media. However, it is important for physicians to be aware of the potential of idiosyncratic paradoxical events when prescribing agents such as cetirizine, particularly to young children less than six years of age.

From the Departments of Pharmacy Practice and Pharmaceutical Sciences, South University School of Pharmacy, Savannah, Georgia.

Reprint requests to Melissa C. Jones, PharmD, BCPS, South University School of Pharmacy, 709 Mall Boulevard, Savannah, Georgia 31406. Email: mjones@southuniversity.edu

Accepted July 28, 2009.

Copyright © 2010 by The Southern Medical Association
0038-4348/0–2000/X00-0001

Case Report

A 23-month-old male was prescribed cetirizine 2.5 mg daily by his attending physician for symptoms of chronic rhinitis. The patient had a history of chronic otitis media from 6 months until 18 months of age treated with multiple antibiotic regimens, ultimately requiring bilateral myringotomy tube placement and adenoidectomy at 13 months of age. On presentation for the chronic rhinitis, he was healthy, had regular sleeping patterns and was on no other therapy or medications. He was prescribed cetirizine daily at bedtime for 14 consecutive days. Within 2–3 days of initiation of the medication, the child began waking regularly throughout the night and remaining awake and restless for extended intervals of time. He would fall asleep and awaken after 2–4 hours of sleep, and remain awake for 1–2 hour intervals. This progressed into the second week of therapy with nocturnal waking intervals lasting from 2–4 hours with sleep intervals shortening to 30–60 minutes in duration. On day 14, the parents discontinued the medication and the child reverted back to a regular, uninterrupted, nocturnal sleep pattern 48 hours following discontinuation of therapy. The child was noted to exhibit a likely idiosyncratic, paradoxical reaction to cetirizine therapy.

Discussion

There are several drug classes used to alleviate allergic symptoms including corticosteroids, antihistamines, decon-

Key Points

- There is limited information regarding the incidence of insomnia in children treated with cetirizine.
- The most common side effects of cetirizine include headache and somnolence.
- Common treatments for allergic rhinitis in children include second-generation oral antihistamines, decongestants, intranasal corticosteroids, mast cell stabilizers, and immunotherapy.

gestants, mast cell stabilizers, anticholinergics, and leukotriene modifiers. In addition, immunotherapy can be used.² Oral antihistamines remain the most commonly used drugs for treatment of this condition. There are two generations of oral antihistamines: the more sedating, first-generation products (i.e. diphenhydramine, brompheniramine) and the nonsedating, second-generation products (i.e., loratadine, cetirizine, and fexofenadine).³ The first-generation products are associated with more central nervous system effects due to their increased potential to penetrate the blood-brain barrier; therefore, the second-generation products are often preferred.

Studies relating adverse effects in children less than two years of age are limited. A prospective, double-blind, parallel-group study was conducted in 817 Canadian children 12 to 24 months old with atopic dermatitis.⁴ The 18-month study randomized patients to cetirizine 0.25 mg/kg (daily dose = 4.35–8.8 mg) or placebo twice daily. While the patient enrollment is considerable for a study of this type, the data reporting of adverse events related to the treatment is confounded and likely overestimated, by the author's own admission, due to the methodology and use of World Health Organization (WHO)-preferred terminology. Insomnia was reported more often in patients receiving cetirizine (35 cetirizine vs 21 placebo; $P = 0.71$). However, investigators, using treatment diaries, attributed the insomnia to teething, itching, or other illnesses. In addition, the overall rate of neurologic symptoms was similar with 65 ($n = 399$) and 55 ($n = 396$) events reported for cetirizine treatment and placebo respectively ($P = 0.373$).

A subsequent study by the same researcher compared the safety of cetirizine to placebo in 85 Canadian infants age 6 to 11 months treated with 0.25 mg/kg twice daily (average daily dose = 4.65 mg) for allergic rhinitis, urticaria, atopic dermatitis, or other conditions for a period of seven days.⁵ Infants in the cetirizine group experienced insomnia at a lower rate than the placebo group (treatment 21.4%, placebo 39.5%; statistical significance not reported). Other clinically significant neurological side effects included nervousness (treatment 28.6%, placebo 41.9%) and somnolence (treatment 19.1%, placebo 27.9%). Treatment diaries noted abnormal

decreases in sleep, restlessness during sleep, and irritability which were more common in patients in the placebo group and more common in the age group of 6 to 8 months.

A Medline search was conducted using the search terms infant, children, cetirizine, and insomnia and resulted in no other case studies describing insomnia related to cetirizine use. Due to the limited clinical studies in children compounded with a treatment population highly prone to sleep disturbances resulting from pathology, the actual rate of treatment-induced insomnia cannot be easily delineated from the present clinical evidence. However, the rate of insomnia in children appears to be comparable to placebo with chronic use.

Insomnia in our patient was attributed to cetirizine due to the onset and resolution coinciding directly with the initiation and discontinuation of the medication. The child exhibited no signs or symptoms of illness or teething and there was no change in his bedtime routine or environment; administration of cetirizine was the only variable element in this patient. Although the reported incidence of insomnia in clinical trials with cetirizine is generally comparable to placebo, it is important for physicians to be aware of the potential of idiosyncratic paradoxical events when prescribing the agent, particularly to young children less than six years of age. If a patient does experience persistent or progressive insomnia, discontinuation followed by challenge with an alternative second-generation antihistamine is a reasonable option.

References

1. Berger WE. Pediatric allergic rhinitis: antihistamine selection. *Clin Pediatr (Phila)* 2005;44:655–664.
2. Seth D, Secord E, Kamat D. Allergic rhinitis. *Clin Pediatr (Phila)* 2007; 46:401–407.
3. Fireman P. Therapeutic approaches to allergic rhinitis: treating the child. *J Allergy Clin Immunol* 2000;105(6 pt 2):S616–S621.
4. Simons FE. Prospective, long-term safety evaluation of the H1-receptor antagonist cetirizine in very young children with atopic dermatitis. ETAC Study Group. Early Treatment of the Atopic Child. *J Allergy Clin Immunol* 1999;104(2 pt 1):433–440.
5. Simons FE, Silas P, Portnoy JM, et al. Safety of cetirizine in infants 6 to 11 months of age: a randomized, double-blind, placebo-controlled study. *J Allergy Clin Immunol* 2003;111:1244–1248.