Oral glycopyrrolate as second-line treatment for primary pediatric hyperhidrosis

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Background: Primary focal hyperhidrosis not uncommonly begins during the first two decades of life, and can have a profound effect on quality of life. Few treatment options have been studied in children.

Objective: We sought to evaluate the response to oral glycopyrrolate in pediatric patients.

Methods: Records of pediatric patients with hyperhidrosis seen at a pediatric hospital in a 10-year period were reviewed retrospectively and, if possible, parents and patients were also interviewed. The efficacy and adverse effects of oral glycopyrrolate were assessed.

Results: In all, 31 children took at least one dose of oral glycopyrrolate. All had daily hyperhidrosis that affected their quality of life and were resistant or intolerant of aluminum salts. The mean age of hyperhidrosis onset was 10.3 years, and mean age of initiation of glycopyrrolate was 14.8 years. At a mean dosage of 2 mg daily, 90% of patients experienced improvement, which was major in 71% of responders. Improvement occurred within hours of administration and disappeared within a day of discontinuation. Duration of treatment averaged 2.1 years (range to 10 years). Side effects were noted by 29% of children, most commonly dry mouth (26%) and eyes (10%), and were dose-related. One patient developed blurred vision, which resolved with dosing below 5 mg/d; one patient experienced palpitations and discontinued the medication.

Limitations: This was a retrospective analysis of a limited number of pediatric patients.

Conclusion: Oral glycopyrrolate is a cost-effective, painless second-line therapy for children and adolescents with primary focal hyperhidrosis that impacts their quality of life. (J Am Acad Dermatol 2012;67:918-23.)

Key words: acetylcholine; adolescence; botulinum toxin; childhood; cholinergic; eccrine; glycopyrrolate; hyperhidrosis; sweat.

Primary focal hyperhidrosis is a disorder of excessive sweating that affects 2.9% of people in the United States.[1] Criteria for diagnosis include focal, visible, excessive sweating of at least 6 months in duration without apparent cause, plus at least two of the following additional features: (1) bilateral and relatively symmetric distribution; (2) at least one episode weekly; (3) impaired daily activities; (4) cessation of focal sweating during sleep; (5) onset before 25 years of age; and (6) family history of primary focal hyperhidrosis.[2] Primary hyperhidrosis is thought to result from a hyperactive sympathetic nervous system, and acetylcholine is the primary transmitter. Palms, soles, and axillae are most often affected.

Although largely considered a problem for adults, primary hyperhidrosis occurs in 1.6% of adolescents and 0.6% of prepubertal children.[1] As in affected

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Funding sources: None.
Conflicts of interest: None declared.
Accepted for publication February 3, 2012.
Reprints not available from the authors.
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Published online March 9, 2012.
0190-9622/$36.00

doi:10.1016/j.jaad.2012.02.012

adults, hyperhidrosis in pediatric patients predominantly localizes to palmoplantar and axillary areas. Primary focal hyperhidrosis can cause considerable emotional and social distress, profoundly affecting quality of life and psychosocial development in pediatric patients.[1,3] Axillary hyperhidrosis wets clothing, requiring frequent changes, and may be associated with an odor; palmar hyperhidrosis interferes with shaking hands and playing sports. In a recent survey, 9 pediatric patients noted difficulty with a range of tasks because of their primary palmar hyperhidrosis, among them writing, handling materials at school, using a computer mouse, holding the handlebar of a bicycle, keeping a notebook dry, keeping hands dry, and playing video games.[3] Hyperhidrosis of the hands and feet has been linked to local desquamation and sometimes pruritic or painful dermatitis. Hyperhidrosis can also increase the risk of cutaneous infections (warts, dermatophytosis, and pitted keratolysis).[4]

CAPSULE SUMMARY

- Primary focal hyperhidrosis can significantly affect pediatric life quality, but few treatment options are available for children who fail to respond to aluminum salts.
- In a retrospective analysis, administration of oral glycopyrrolate (mean 2 mg/d) improved the hyperhidrosis in 90% of 31 treated children. Tolerable dry mouth or eyes was noted in 26%, but one patient discontinued treatment because of palpitations.
- Oral glycopyrrolate is a cost-effective, painless, well-tolerated second-line therapy for pediatric hyperhidrosis.

Therapeutic options are limited for hyperhidrosis in children and adolescents (for reviews[5,6]). First-line intervention typically involves topical application of aluminum salts, but their use is limited by potential local irritation and short duration of action. Topical applications can also be messy and time-consuming, leading to decreased adherence, particularly in children.[5] Local injections of botulinum toxin A have more recently been introduced as a second-line option before considering iontophoresis or surgical denervation. However, botulinum toxin injections are painful without regional anesthetic blockade and quite costly. Furthermore, treatment of hyperhidrosis at multiple sites, which occurs in the majority of affected individuals, requires serial or combination treatments. Thoracic sympathectomy has been reserved for hyperhidrosis unresponsive to other treatments.

An often forgotten treatment approach for pediatric hyperhidrosis is oral administration of glycopyrrolate, an inexpensive anticholinergic agent that has often been prescribed for children with excessive salivation. We performed a retrospective analysis of the efficacy and observed side effects associated with oral glycopyrrolate used for hyperhidrosis at a single pediatric referral center during the past 10 years.

METHODS

After approval by the Institutional Review Board at Children's Memorial Hospital/Northwestern University, Chicago, IL, the charts of all 3- to 17-year-old patients for whom the *International Classification of Diseases, Ninth Revision* code corresponded to focal (705.2) primary hyperhidrosis were systematically reviewed. All patients had been personally evaluated by a board-certified pediatric dermatologist. Patients with hyperhidrosis for less than 6 months or with generalized or secondary hyperhidrosis were excluded. The charts of patients who had used oral glycopyrrolate for at least one dose and returned in follow-up were further reviewed to assess age, gender, disease characteristics, treatment history, dosage of glycopyrrolate, response, and observed adverse effects.

An attempt was made to contact parents of patients in the study (or patients themselves if now ≥ 18 years of age) to obtain additional medical information by telephone interview or in person after verbal consent. Hyperhidrosis was rated historically as mild, moderate, or severe, based on the frequency of excessive sweating and extent of interference with daily activities. "Mild" was defined as excessive sweating that was only associated with specific triggers, such as nervousness, and minimally interfered with daily activities. "Moderate" was defined as excessive sweating without specific triggers that only occasionally interfered with activities. "Severe" was defined as excessive sweating on a daily basis that led to major avoidance of activities. The improvement was rated as "major" or "adequate" based on chart documentation or verbal interview.

RESULTS

Records for 159 pediatric patients with the diagnosis of hyperhidrosis who were seen between January 2001 and December 2010 were available for review. Of these patients, 31 (19%) were determined to have severe hyperhidrosis at presentation (interfered with activities daily) and had been administered at least one dose of oral glycopyrrolate. All of these pediatric patients were confirmed to