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## Craniofacial Hyperhidrosis Successfully Treated With Topical Glycopyrrolate

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### Abstract and Introduction

#### Abstract

Treatment of craniofacial hyperhidrosis currently consists of thoracic sympathectomy, which is not widely available. Oral anticholinergic agents and  $\beta$ -blockers may be effective but also carry significant side effects. We describe a healthy, active 27-year-old male resident physician who had excessive facial sweating with minimal exertion or stress. The sweating was especially pronounced on the forehead, nose, and upper lip. Daily topical application of a 0.5% glycopyrrolate solution to the face and forehead was offered. After the first treatment, facial sweating was significantly reduced and was well controlled under stressful situations, without any discomfort to the skin. No loss of efficacy was seen after multiple face washings. Facial hyperhidrosis recurred after withdrawal of the glycopyrrolate for 2 days, confirming its therapeutic effect. Two years later, he continues to use glycopyrrolate as needed. We conclude that topical glycopyrrolate is effective in treating craniofacial hyperhidrosis and is associated with few adverse effects.

#### Introduction

Eccrine sweat glands primarily assist the body in regulating its temperature in response to heat exposure or exercise. In about 1% of the population, the sympathetic nervous system is overactive, causing certain areas of the body to sweat at inappropriate times and beyond what is necessary to maintain thermal regulation. This disorder is known as primary hyperhidrosis.<sup>[1]</sup> Although primary or essential hyperhidrosis is not usually a cause of major morbidity, it presents an occupationally disabling and socially embarrassing problem to those afflicted with it. Most commonly, hyperhidrosis appears on the palms, but also appears on the face, soles of the feet, and the axillae. The causes of secondary hyperhidrosis include a number of neoplastic and neurologic disorders, metabolic diseases, and drugs. These causes should be identified and treated accordingly.

Craniofacial hyperhidrosis has been a clinical problem overshadowed by palmar, plantar, and axillary hyperhidrosis. Nevertheless, craniofacial hyperhidrosis is a psychologically and socially distressing problem that has received limited attention by the antiperspirant industry and the medical community alike. Reports dealing with craniofacial hyperhidrosis have been few, compared with studies aimed at treating axillary or palmar hyperhidrosis. The following case describes a significant reduction of facial hyperhidrosis after local application of a topical formulation of glycopyrrolate 0.5% in aqueous solution.

#### Case Report

A healthy, active 27-year-old male resident physician with no medical history complained of excess facial sweating with minimal exertion or stress. The sweating was especially pronounced on his forehead, nose, and upper lip. He had previously seen a dermatologist who prescribed an aluminum chloride roll-on solution. Discomfort associated

with feeling as if a "film" were covering his face as well as limited duration of action and total loss of efficacy after washing his face were reasons given for discontinuing the use of aluminum chloride.

Daily topical application of a 0.5% glycopyrrolate solution to the face and forehead was offered. The solution was supplied as a roll-on to be applied at bedtime. He was instructed to wash his face with soap and water before application to ensure optimal absorption. After the first treatment, he noticed a significant reduction in facial sweating. Under stressful situations (ie, being called on in morning report and placing a central venous catheter during a "code blue"), the facial sweating was well controlled without any discomfort to the skin. No loss of efficacy resulted from multiple face washings. Recurrence of facial hyperhidrosis after 2 days without using the glycopyrrolate confirmed its therapeutic effect. After about 1 month of use, compensatory sweating was noted at his temples. This was subsequently controlled by his applying additional solution to these areas. Two years later, he continues to use glycopyrrolate and reports excellent control of facial sweating. He has also reported that the solution is effective for controlling sweating around the neck.

## Discussion

Treatment of primary hyperhidrosis remains challenging. Topical agents used include aluminum chloride, potassium permanganate, glutaraldehyde, and formaldehyde, but their effects are only short-term.<sup>[2]</sup> Oral anticholinergic agents have also been used, but these have many undesirable systemic side effects such as blurred vision, tachycardia, and urinary retention.<sup>[3]</sup> Tranquilizers such as diazepam,<sup>[1]</sup> as well as central-acting  $\alpha$ -adrenergic agonists such as clonidine<sup>[4,5]</sup> have been used but are limited by their neurocardiovascular side effects. Although  $\beta$ -blockers have been used to treat sweating associated with anxiety,<sup>[6]</sup> their effectiveness in primary hyperhidrosis lacks support from the literature. Surgical excision of affected areas has been useful in some cases<sup>[7]</sup> but is generally limited to the axillae. Although endoscopic sympathectomy has a success rate of 92% to 99%, the complications are significant and include permanent Horner's syndrome, compensatory hyperhidrosis, gustatory sweating, hemothorax, intercostal neuralgia, and cardiac sympathetic denervation.<sup>[1]</sup> Iontophoresis has been shown to successfully control palmar and plantar sweating via a mechanism thought to be due to poral plugging.<sup>[8]</sup> Finally, subcutaneous botulinum toxin injections have also been praised as a desirable treatment option for the palms,<sup>[9]</sup> axillae,<sup>[10]</sup> and forehead,<sup>[11]</sup> but they are associated with high cost and painful injection and can result in neurologic impairment such as a weakened hand grip or weakness of forehead muscles.

Sympathetic outflow to the skin includes cholinergic neurons innervating sweat glands and adrenergic neurons innervating blood vessels and hair follicles (vasoconstrictor and pilomotor neurons). Cutaneous vasomotor activity causing facial sweating is mediated by T2 to T3 segments of the spinal cord via the superior cervical ganglion. Postganglionic axons accompany branches of the internal carotid (innervating sweat glands and vessels of the forehead), and the axons traveling along the external carotid artery innervate the rest of the face and follow branches of the trigeminal nerve.<sup>[12]</sup>

Topical anticholinergics are an attractive option that have been shown to be effective for the treatment of Frey's syndrome of gustatory sweating after parotidectomy,<sup>[13]</sup> primary craniofacial hyperhidrosis,<sup>[14]</sup> and diabetic gustatory sweating.<sup>[15]</sup> Glycopyrrolate is a quaternary ammonium anticholinergic agent similar to atropine that inhibits the action of acetylcholine on structures innervated by postganglionic cholinergic nerves. Unlike atropine or scopolamine, the occurrence of central nervous system related side effects is minimal, because the quaternary ammonium group of glycopyrrolate limits its passage across lipid membranes such as the blood brain barrier.<sup>[16]</sup> The sweat gland activity of glycopyrrolate is similar to that of atropine, but more prolonged. On a molar basis, glycopyrrolate is about 5 to 6 times as potent as atropine.<sup>[17]</sup> Since eccrine sweat gland secretion is cholinergically mediated, the ability to inactivate secretion via direct cholinergic receptor blockade appears more attractive than merely occluding sweat ducts with aluminum chloride or iontophoresis.

The first clinical trial of topical glycopyrrolate in patients with Frey syndrome involved more than 1,000 individual applications with only seven cases of minor side effects.<sup>[18]</sup> Three subsequent clinical trials using topical glycopyrrolate<sup>[13,19,20]</sup> showed no side effects associated with its use, with the exception of one patient who had a local eczematous reaction.<sup>[19]</sup> Three individual case reports<sup>[14,15,21]</sup> showed that topical glycopyrrolate was well tolerated when used on the face, and there were no reported side effects.

## Conclusion

The use of topical glycopyrrolate, a quaternary anticholinergic, appears to be effective in the treatment of

craniofacial hyperhidrosis and is associated with few adverse effects.

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## Sidebar: Key Points

- Current treatments of craniofacial hyperhidrosis carry significant side effects or are ineffective.
- Glycopyrrolate, a quaternary anticholinergic, "turns off" the sweat gland via cholinergic blockade, instead of occluding sweat pores.
- Topical glycopyrrolate is an effective treatment of primary craniofacial hyperhidrosis associated with few side effects.

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