

Treatment of Compensatory Gustatory Hyperhidrosis with Topical Glycopyrrolate

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Gustatory hyperhidrosis is facial sweating usually associated with the eating of hot spicy food or even smelling this food. Current options of treatment include oral anticholinergic drugs, the topical application of anticholinergics or aluminum chloride, and the injection of botulinum toxin. Thirteen patients have been treated to date with 1.5% or 2% topical glycopyrrolate. All patients had gustatory hyperhidrosis, which interfered with their social activities, after transthoracic endoscopic sympathectomy, and which was associated with compensatory focal hyperhidrosis. After applying topical glycopyrrolate, the subjective effect was excellent (no sweating after eating hot spicy food) in 10 patients (77%), and fair (clearly reduced sweating) in 3 patients (23%). All had reported incidents of being very embarrassed whilst eating hot spicy foods. Adverse effects included a mildly dry mouth and a sore throat in 2 patients (2% glycopyrrolate), a light headache in 1 patient (1.5% glycopyrrolate). The topical application of a glycopyrrolate pad appeared to be safe, efficacious, well tolerated, and a convenient method of treatment for moderate to severe symptoms of gustatory hyperhidrosis in post transthoracic endoscopic sympathectomy or sympathectomy patients, with few side effects.

Key Words: Hyperhidrosis, gustatory, glycopyrrolate, sympathectomy

INTRODUCTION

Gustatory hyperhidrosis is often a disabling and embarrassing sequela after endoscopic transthoracic sympathectomy (or sympathectomy). Most

patients are not troubled by sympathectomy.¹ However, about 75% of patients experience compensatory hyperhidrosis, and approximately 10-36% of patients gustatory hyperhidrosis.^{2,3} Few consider this condition to be a major problem in daily life. Unfortunately, there is no way of predicting the severity of the condition. Gustatory hyperhidrosis is a facial sweating, usually associated with the eating of hot spicy food or even the smelling of such food, and the condition may present time soon after the surgical procedure or even years later. Unfortunately for these patients, spicy food is a main and essential component of the Korean diet, and patients feel like social outcasts when faced with spicy food. Moreover, patient discomfort during more formal occasions, like a dinner party, may cause profuse sweating. For this reason patients tend to avoid certain social activities, which can lead to frustration, anger, stress and depression.

Currently, treatment options for gustatory hyperhidrosis include oral anticholinergic drugs, the topical application of anticholinergics or aluminum chloride, or the injection of botulinum toxin. The latter of which requires the identification of the sweating area and is well tolerated, with no important side effect. Botulinum toxin treatment produces predictable, controllable, long lasting results that can be easily reproduced. Its minor transient side effects are pain at the injection site, equimosis, an allergic reaction to the albumin, and ptosis palpebral. However, the high cost of treatment is a limiting factor and the main obstacle to treatment advancement. Aluminum chloride has been shown to be effective for use at the axillae, palm and sole. However, rashes, stinging sensations and irritation to the skin pre-

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vent its use on the face. Systemic anticholinergics may be effective, but they have a poor side effect profile in some of patients and are unappealing in focal hyperhidrosis. Patients often find systemic agents ineffective at abolishing their hyperhidrosis, causing them to search for other options.

Several studies have shown that the topical anticholinergic, glycopyrrolate, is very effective in the management of gustatory hyperhidrosis, and this treatment is available in many forms (roll-on lotion, cream, solution) for gustatory hyperhidrosis in diabetic patients.^{4,6} One study reported that craniofacial hyperhidrosis was successfully treated with topical glycopyrrolate.⁷ We have experienced patients who were successfully treated for severe and distressing gustatory hyperhidrosis using the anticholinergic agent, glycopyrrolate, applied topically instead of orally. In addition, we successfully treated 13 patients with gustatory hyperhidrosis after transthoracic endoscopic sympathectomy using this treatment with few adverse effects.

MATERIALS AND METHODS

A clinical trial of topical commercially available 1.5% or 2% glycopyrrolate pads (www.pharmacy.ca, Securetm, Toronto, Canada) was performed in 13 patients between November 2002 and January 2003. All patients in Table 1 were given a complete explanation as how to apply the topical glycopyrrolate and its possible complications. Signed written informed consent was obtained from all subjects. Patients were asked to telephone or e-mail us if they noticed side effects. Patients were selected according to the following criteria: gustatory hyperhidrosis of more than 5 months duration as a major complication, a history of sympathectomy or sympathicotomy, the lack of an alternative treatment option (oral anticholinergics are not available in Korea at the time of writing, and botulinum toxin is too expensive for many patients), non-clinical depression after surgery.

After careful history taking and a physical examination (objective evaluations such as, Minor's iodine starch test, a gravimetric or a hygrometric test, and a colorimetric test were not conducted), subjective diagnosis was made by history and

visible signs of sweating after eating spicy foods. Measurements of, blood pressure, routine blood chemistry, and thyroid function test were performed in each patient to rule out other causes of hyperhidrosis. Each patient was instructed to clean the affected area once daily and to apply topical glycopyrrolate, avoiding contact with the eyes, nose and mouth. Patients were allowed to apply cosmetics and to wash 4 hours later as required. The pads were used either on a regular basis, or if a patient preferred, prior to social activity. Each pad was used for 2 days to treat excessively sweating areas. Patients were asked to return after 2-3 weeks. On the return visit, patients' subjective observations and experiences were evaluated.

RESULTS

Thirteen patients were treated with topical glycopyrrolate. All patients had gustatory hyperhidrosis that interfered with social activity after transthoracic endoscopic sympathectomy and this was associated with compensatory focal hyperhidrosis. Six males and 7 female subjects aged from 15 to 35 years participated (Table 1). The areas mainly affected by gustatory hyperhidrosis were, the forehead, frontal and occipital head, para nasal area, cheek and above the upper lip. The applied concentration was 1.5 or 2%. After applying topical glycopyrrolate, the subjective effects were, excellent (no sweating after eating hot spicy food) in 10 patients (77%), and fair (clearly reduced sweating but small amount remained) in 3 patients (23%). All patients felt symptom free after applying the pads, and all had enjoyed eating hot spicy foods that they were previously afraid of eating.

Adverse effects included; a mild dry mouth and sore throat in 2 patients (2% glycopyrrolate) and a light headache in 1 patient (1.5% glycopyrrolate). Skin irritation and other adverse reactions were not encountered. The drugs were well tolerated throughout the treatment session without specific complaint. Eleven out of the 13 patients who completing the trial wished to continue using the topical drug. One subject did not want to continue the treatment for personal reasons, and

Table 1. Characteristics of the Patients

Patients No.	Sex	Age (years)	Duration of symptoms (months)	Associated sweating region	Concentration used (%)
1	M	23	12	chest, axilla	1.5%
2	F	15	5	right arm, sole	1.5%
3	F	30	11	none	1.5%
4	F	21	14	back, axilla	1.5%
5	F	19	18	chest, abdomen, buttock	1.5%
6	M	22	8	sole	2.0%
7	M	28	9	sole	1.5%
8	F	26	11	chest, sole	1.5%
9	F	35	6	chest, back	1.5%
10	M	28	14	lower half of body	2.0%
11	M	27	16	chest, back, sole	2.0%
12	M	20	9	abdomen, buttock	1.5%
13	F	26	17	whole body except abdomen	1.5%

the other experienced facial flushing for a short period after application.

DISCUSSION

Gustatory hyperhidrosis is not a rare manifestation post transthoracic endoscopic sympathectomy. Approximately one third of patients report experiencing gustatory hyperhidrosis post sympathectomy.² Diabetic neuropathy also causes gustatory hyperhidrosis⁶ and Frey's syndrome (damage to the auriculotemporal nerve after parotidectomy and the results of a regeneration of nerve fiber, respectively) are other common causes of gustatory hyperhidrosis, which presented as unilateral sweating and not bilateral sweating as in patients of diabetes mellitus.⁸ Though the mechanism is unclear, most likely mechanism is presumed to involve the aberrant reinnervation of facial sweat glands due to a severed thoracic (or trunk) sympathetic ganglion.

Currently various therapeutic and preventive options for gustatory hyperhidrosis have been advocated, as this condition remains a challenging domain. Moreover, therapy can be challenging for the patient and for the physician. People who suffer from excessive sweating often feel frustration that the root cause is not found a specific

treatment. Treatment options include topical and systemic medications, and injection of botulinum toxin.

Botulinum toxin injection is a newer therapeutic modality. The mechanism of action stems from its anticholinergic effects at the neuromuscular junction and in the postganglionic sympathetic cholinergic innervation of the sweat glands. These injections have to be repeated at varying intervals in order to achieve long-term results.^{8,9} Botulinum toxin is simple to inject, based on the Minor's test. The duration of results exceeds 4 months and may be permanent in some patients.¹⁰ The cost of medication and minor adverse effects such as, injection pain, minor hematoma and weakness of the forehead muscle are the only limiting clinic factors.

Oral anticholinergics have been used for compensatory hyperhidrosis for more than two decades. Propantheline, glycopyrrolate, oxybutynin and benztropine may be effective.¹¹ Anticholinergics act by preventing acetylcholine, released from the ends nerve fibers, from stimulating sweat gland receptors. Glycopyrrolate shields the sweat gland from the action of acetylcholine and does not cross the blood brain barrier, unlike other anticholinergics. Therefore, glycopyrrolate is less likely to produce side effects. Sometimes a dry mouth becomes a major problem and leads to

discontinuance.

Topical therapies applied to the skin are practical in use and are commonly treatments of choice. Topical chemicals include aluminum chloride, scopolamine, potassium permanganate, glutaraldehyde, formaldehyde, and glycopyrrolate. However, many of these agents, which have been proven useful in clinical trials, are unavailable commercially. The most popular agent has been glycopyrrolate, which causes much less facial discomfort. Shaw demonstrated that topically applied glycopyrrolate is very effective at reducing both the severity and frequency of diabetic gustatory hyperhidrosis.⁴ Also a topical formulation of glycopyrrolate, 0.5% in aqueous solution, was reported to be effective at treating craniofacial hyperhidrosis and to be associated with few adverse effects.^{5,7} We used 1.5% or 2% topical glycopyrrolate that was impregnated in pads, allowing the agent to be simply wiped onto the skin. Controlling gustatory sweating is achieved by the slow penetration of high concentrations of the active agent in the area of the sweat glands, and the topical application ensures that only very low concentrations are reached in the systemic circulation. Thus, undesirable effects such as mouth dryness are uncommon. In the present study, three cases of minor side effects occurred. Efficacy was maintained for 2 days by a single pad, and treatment did not interfere with daily washing; facial sweating returned after withdrawing the agent.

In summary, topical application using the glycopyrrolate pad appears a safe, efficacious, well tolerated, and convenient treatment for moderate to severe symptoms of gustatory hyperhidrosis in post transthoracic endoscopic sympathectomy

or sympathectomy patients, with few side effects.

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