Oral Medications

Dee Anna Glaser, MD

KEYWORDS

• Systemic therapy • Anticholinergic • β-blocker • Glycopyrrolate • Oxybutynin • Propanolol • Clonidine • Hyperhidrosis

KEY POINTS

- Localized treatments for hyperhidrosis are considered first-line therapy.
- Systemic therapy can be used as monotherapy or in combination with focally targeted treatments.
- Anticholinergic drugs are the most commonly used systemic therapy for hyperhidrosis.
- Side effect profiles of anticholinergic drugs vary based on their lipid solubility.
- β-Blockers can be useful for hyperhidrosis associated with performance tasks.
- There is a paucity of published literature on systemic treatment of hyperhidrosis.

INTRODUCTION

Hyperhidrosis (HH) is a disabling condition that impacts quality of life (QOL) and can cause significant emotional stress. Primary HH presents with focal areas of excess sweating, such as the axillae, palms, soles, scalp, face, and groin. Although some patients have only one focal area of excessive sweating, it is common for patients to have more than one body site producing excessive amounts of sweat.[1] In addition, patients may present with more generalized forms of HH, which are usually secondary in nature. In these cases, treatment or removal of the offending cause is beneficial, but may not always be feasible. Compensatory HH following sympathectomy varies significantly but occurs in 50% to 80% of patients who undergo sympathectomy.[2] It can affect very large areas, such as the chest, abdomen, and back, and is irreversible. Systemic therapy can be beneficial in all of these patients.

None of these agents have a Food and Drug Administration–approved indication to treat HH and there is a paucity of literature or studies on the use of these medications for the treatment of HH.

TREATMENT INDICATIONS

In general, treatment of primary HH should be as specific and focal or localized as possible to ensure good response and minimize side effects and interactions with other medications. Topical therapies are usually first-line treatment, and then more focally targeted therapies, such as botulinum toxin injections, iontophoresis, or microwave thermolysis, should be considered. However, when these treatments are ineffective, intolerable, or not feasible, systemic therapies are a good option. Oral medications can be added to the previously mentioned treatments to enhance improvements. This is especially beneficial when patients have multiple areas of HH. I might use botulinum toxin A injections for the axilla and iontophoresis for the hands and feet, but have to add an oral agent to manage such areas as the groin, face, or submammary sweating.

Generalized sweating presents a challenge. If a specific cause is identified, that agent or cause should be removed. However, it is common that an offending agent cannot be removed. Patients with psychiatric disease frequently cannot lower or change the medications that are controlling their

Disclosure: D.A. Glaser has served as advisor for Allergan, Galderma, Miramar Labs, and Unilever. She has been an investigator and received research grants from Allergan, Miramar Labs, and Ulthera.
Department of Dermatology, Saint Louis University School of Medicine, 1402 South Grand Boulevard-ABI, St Louis, MO 63104, USA
E-mail address: glasermd@slu.edu

Dermatol Clin 32 (2014) 527–532
http://dx.doi.org/10.1016/j.det.2014.06.002
0733-8635/14/$ – see front matter

mental illness. In these instances, other options, such as oral medications to treat the HH, have to be considered.[3] Some patients have multiple cofounding factors that can induce or worsen HH, and in these patients oral therapy may be very helpful.

There are groups of patients that should be considered very carefully before initiating therapy with oral medications, especially the oral anticholinergics, which decrease sweating from the entire body. Athletes and individuals who work or play a lot outdoors may become overheated if they are unable to cool their bodies without sweat evaporation, and may have an increased risk of hyperthermia and heat stroke. Small children or individuals who have difficulty self-monitoring their body temperature, mentation, and urine output may not be good candidates for oral anticholinergics. Allergies, other medications, or health issues need to be reviewed to avoid interactions or worsening of other diseases or health concerns. As an example, β-blockers are generally not given to patients with psoriasis.

It is very important to counsel patients on what therapy you are using, how it works, and what to monitor. It is also critical that patients are counseled on realistic expectations. Most patients can expect an improvement but not complete resolution of their HH symptoms. I counsel patients that they will most likely still have episodes of sweating when others around them do not, and that they will most likely still be the first to sweat and even sweat more than their counterparts during activity. Setting a step-wise plan for the patient can also be helpful so that they do not discontinue therapy and understand that if a plan is not providing enough improvement, then the next step will be added, especially with oral therapies. Improvement in symptoms is usually possible to achieve, but anhidrosis is not, nor is it desirable.

ANTICHOLINERGIC AGENTS

Because the sweat glands are innervated by the sympathetic postganglionic nerves and have acetylcholine as the primary neurotransmitter, the use of anticholinergic agents is a logical choice to treat HH.[4] Anticholinergic agents work by competitive inhibition of acetylcholine at the muscarinic receptor. Muscarinic receptors are present throughout the central and autonomic nervous system, accounting for widespread and varied side effects that can develop.

There are several anticholinergic agents; however, there are differences in the side effect profile. Glycopyrrolate is a quaternary amine with limited passage across lipid membranes, such as the blood-brain barrier. This is in contrast to such agents as atropine or scopolamine, which are tertiary amines and can easily penetrate lipid barriers. This is probably the reason why glycopyrrolate has fewer central nervous system side effects and may have less effect on the heart rate at lower doses.[5] The most common side effect is dry mouth caused by inhibition of salivary glands. There are many potential side effects (**Box 1**) and concurrent use with other medications with anticholinergic activity, such as phenothiazines, antiparkinson drugs, or tricyclic antidepressants, intensifies the antimuscarinic effects and increases side effects. Anticholinergic therapy may be contraindicated in patients with glaucoma, obstructive uropathy, obstructive diseases of the gastrointestinal (GI) tract, paralytic ileus, severe ulcerative colitis, and myasthenia gravis.

Glycopyrrolate

Glycopyrrolate is the author's most commonly used anticholinergic drug to treat HH. Dosing is variable and is usually started at 1 to 2 mg twice daily (BID). The patient is asked to increase the dose by 1 mg per day at 2-week intervals based on the therapeutic response and side effects. Dry mouth is the most common side effect and usually the limiting factor in dosing. If side effects are minimal, management can allow patients to continue their medication. Managing dry mouth could include use of artificial saliva preparations, increasing water intake, and keeping candy or mints available; increased fiber consumption and light exercise can help to improve mild constipation. Over-the-counter eye drops can improve dry eye symptoms, but many patients have to discontinue therapy because of intolerable side effects. The efficacy and side effects of therapy are generally dose-dependent.

Walling[6] published a retrospective review of 45 patients who used glycopyrrolate to treat HH of various body sites. Overall 67% were responders and 33% failed treatment. Of the treatment failures, 40% were nonresponders and the rest had adverse effects requiring medication cessation (xerostomia, GI disturbance, headache, rash, and mental status change). Only one-fourth of his patients used it as monotherapy, but others combined therapy with topical aluminum chloride, botulinum toxin, and iontophoresis. His patients most commonly took 1 mg daily and the highest dose that was used was 6 mg daily. Bajaj and Langtry[5] reported on 19 patients treated with glycopyrrolate and found that 80% responded to therapy. The most common dose was 2 mg BID or three times daily (TID) but one patient took