ANTICHLINERGIC DRUGS IN THE TREATMENT OF FACIAL HYPERHYDROSIS: A REVIEW ARTICLE

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ABSTRACT

Background: Hyperhidrosis is a disorder characterized by excessive sweating. It is a common health problem affecting about 3% of the population. Facial hyperhidrosis is a frequent complaint which usually affects the forehead bilaterally but can also involve other regions of the face such as the scalp, nose, chin and less frequently cheeks. There are many available treatments for facial hyperhidrosis including systemic treatment as anticholinergic drugs, topical antiperspirants as topical 20% aluminum chloride and surgical management.

The aim of this article is to review the efficacy and safety of anticholinergic drugs such as botulinum toxin A, topical glycopyrrolate and oxybutynin in the treatment of facial hyperhidrosis.

Methods: An extensive literature review was conducted by searching PubMed, Medline, and ClinicalKey to find articles about using anticholinergic drugs in the treatment of facial hyperhidrosis.

Results: The outcomes and results were compiled for cases of facial hyperhidrosis treated with anticholinergic drugs.

Conclusion: Based on the available evidences, topical glycopyrrolate, oxybutynin and botulinum toxin A should be considered as first-line therapies of facial hyperhidrosis due to their efficacy and safety.

Keywords: facial hyperhidrosis, excessive sweating, glycopyrrolate, oxybutynin, botulinum toxin

I. INTRODUCTION

Facial hyperhidrosis is a frequent complaint which usually affects the forehead bilaterally but can also involve other regions of the face such as the scalp, nose, chin and less frequently cheeks. It can be either focal affecting only the face and scalp or part of a generalized hyperhidrosis involving several body sites of skin. It could be primary or secondary to other causes such as infection, endocrine disturbance or neoplasm [1]. Primary facial hyperhidrosis is characterized by sudomotor dysregulation stimulated by triggers such as heat and stress. The cause of primary facial hyperhidrosis could be excessive stimulation of the sweat glands by an overactive sympathetic system or by overreaction of the glands to a normal amount of acetylcholine [2].

Available treatments for facial hyperhidrosis

There are many available treatments for facial hyperhidrosis including systemic treatment as anticholinergic drugs, topical antiperspirants as topical 20% aluminum chloride and surgical management. The main systemic agents used to treat facial hyperhidrosis are anticholinergic agents (Table 1). Anticholinergic drugs are classified either as nicotinic receptor antagonists or as muscarinic receptor antagonists, depending on acetyl choline receptor specific binding [3]. Anticholinergic drugs act directly on the nerves in the sweat glands to show a perspiration suppression effect. However, they suppress the sympathetic nervous system, so symptoms as oral dryness, palpitations, constipation, dysuria, digestive problems, dizziness, and headaches may occur. So, they cannot be used in patients with underlying diseases such as cataracts or urologic disease. Despite these disadvantages, anticholinergic drugs are still the most frequently selected medication for many diseases [4]. A systematic review was published by Nicholas et al (2015) on treatment of primary craniofacial hyperhidrosis and...
stated that topical glycopyrrolate, oral oxybutynin and intradermal botulinum toxin A are the first-line therapies due to their efficacy and safety [2]. Very few reports were then published on treatment of facial hyperhidrosis with botulinum toxin A, topical glycopyrrolate and oxybutynin as illustrated in that may attributed to paucity of cases or because the patients did not know that it is a treatable condition as some patients stated in the study.

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of study</th>
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<th>results</th>
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</thead>
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<tr>
<td>Kinkelin et al [7]</td>
<td>Prospective, uncontrolled</td>
<td>10</td>
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<td>100% success rate</td>
</tr>
<tr>
<td>George et al [8]</td>
<td>Case study</td>
<td>4</td>
<td>Botulinum toxin injection</td>
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</tr>
<tr>
<td>Kim et al [15]</td>
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<tr>
<td>Hyun et al [16]</td>
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<td>2% glycopyrrolate</td>
<td>significant reduction in sweat production in the glycopyrrolate-treated half of the forehead</td>
</tr>
<tr>
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<td>Oral oxybutynin</td>
<td>80% success rate</td>
</tr>
<tr>
<td>Wolosker et al [22]</td>
<td>prospective, non randomised, uncontrolled</td>
<td>61</td>
<td>Oral oxybutynin</td>
<td>100% success rate</td>
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</tbody>
</table>

**Role of botulinum Toxin in treatment of facial hyperhidrosis**

Botulinum Toxins (BTX) are produced by various strains of Clostridium botulinum, anaerobic Gram positive spore forming bacilli [5]. Commercially available Botulinum Toxins are botulinum toxin type A (BTA) and botulinum toxin type B (BTB). BTA and BTB have light and heavy chain connected with disulfide bond. Light chain of BTA bond with 5-Kd synaptosome-associated protein (SNAP-25), a protein which plays a major role in acetylcholine secretion from vesicles in the nerve ending. Light chain of BTB bond is less specific so BTA is more effective than BTB. BTX type A (BTX-A) has been approved by the US FDA for the treatment of axillary hyperhidrosis and is often used off-label for the treatment of palmar, plantar, and craniofacial hyperhidrosis[6]. Botulinum toxin inhibits sweat production from the eccrine glands by blocking acetylcholine release at the neuromuscular junction from cholinergic fibres[7]. Although the use of botulinum toxin for axillary hyperhidrosis is well established and used worldwide, its use in facial sweating is very limited and little literature detailing the dosage, technique and practical considerations are available and mostly published by non-dermatologists[8]. Boger et al (2000) was the first to report the use of botulinum toxin A in the treatment of idiopathic craniofacial hyperhidrosis after its successful use in treatment of gustatory hyperhidrosis [9]. Kinkelin et al assessed the response to treatment with botulinum toxin A in 10 men suffering from frontal hyperhidrosis. Three units of botulinum toxin A were injected intracutaneously over the forehead with a distance ranged from 1 to 15cm between 2 points. The amount of sweat was significantly reduced, 4 weeks after treatment in all patients, with minor side effects [7]. Komerciki and Ardjomand (2012) also published a case report of treatment of the whole face hyperhidrosis with botulinum toxin A. They stated that injections of very small amounts with very short distances between the injection sites were highly successful and avoid diffusion to muscles [10]. George et al (2014) reported successful treatment of hyperhidrosis in different sites of the face in 4 cases with 2 units of botulinum toxin A per injection. No side effects have occurred in cases with upper and middle face hyperhidrosis (3 cases). The fourth case (lower face) suffered from dropping of the left upper lip that could be due to high dose of the toxin [8]. Injections with botulinum toxin are generally well tolerated and side effects are few and the most feared adverse effect is temporary unwanted weakness/paralysis of nearby musculature[11].

**Role of glycopyrrolate in the treatment of facial hyperhidrosis**

Glycopyrrolate (GPB) is among the most common anticholinergic medications[12]. Primary mechanism of action of glycopyrrolate is the blockage of acetylcholine's effects at the parasympathetic sites in various tissues. This blockage primarily occurs in the central nervous system, smooth muscle, and sebaceous glands [13]. Glycopyrrolate has been recommended as second to third line therapy for severe hyperhidrosis involving the palms, soles, or axillae, and as one of several first-line options for craniofacial hyperhidrosis [14]. Topical formulations such as creams and shower lotions containing 0.5—2% GPB, were investigated as a treatment for primary hyperhidrosis. Recently, topical glycopyrroinum received approval by the U.S. Food and Drug
Administration (FDA) for the treatment of primary axillary hyperhidrosis [3]. It may be applied on a daily basis or before certain occasions, such as prior to social activities. Although topical glycopyrrolate is convenient to use, the limitation is that the effects lasted only 1 or 2 days in response to a single application [15]. The effect of Glycopyrrolate on the treatment of facial hyperhidrosis was investigated in some studies. Kim et al. (2008) enrolled 25 patients with facial hyperhidrosis whom were treated with single application of 2% topical glycopyrrolate on one-half of the forehead, whereas the other half of the forehead was treated with a placebo. Most patients were greatly relieved after treatment. Sweat reduction was significant according to gravimetric assessment, with good short-term results [15]. Also, Hyun et al. (2015) treated forehead hyperhidrosis in 39 participants with 2% glycopyrrolate in a placebo controlled study once a day for 9 successive days. They showed significant reduction in sweat production in the glycopyrrolate-treated half of the forehead and a measurable decrease in sweat was decreased, as the number of daily applications increased during this study [16]. Adverse reactions after glycopyrrolate administration included anticholinergic symptoms such as mydriasis, hyperthermia, tachycardia, and cardiac arrhythmia. They may also include blurred vision, constipation, cycloplegia, dry mouth, dry skin, flushing, photophobia, and xerophthalmia [15]. Although topical application is often used to avoid systemic side-effects, it can result in contact sensitization. It can affect cholinergic nerve endings that may lead to systemic absorption and adverse effects [4]. Local skin reactions with glycopyrrolumtosylate were observed in some studies [17].

**Oxybutynin efficacy and safety in treatment of facial hyperhidrosis**

Oxybutynin is an anticholinergic drug able to antagonize the M1, M2, and M3 subtypes of the muscarinic receptors [18]. According to the Canadian Hyperhidrosis Advisory Committee, it is considered as first-line therapy for craniofacial hyperhidrosis and primary extensive hyperhidrosis [19]. Oxybutynin effect on hyperhidrosis was first investigated in 1988 [20]. After that it has been increasingly used as an initial or alternative therapy, especially in elderly who are not candidates for surgery, or in patients with primary extensive hyperhidrosis. Over the years, several studies investigated its effects on facial hyperhidrosis. In a non-randomized and uncontrolled study of 19 individuals with facial hyperhidrosis, most of them over forty years old, the authors reported an overall improvement of 75% with great improvement in 52% [21]. Another trial reported the long-term results of facial hyperhidrosis in sixty one subjects who showed maintenance in the improvement level experienced in the first 12 weeks in over 95% of the patients [22]. These studies demonstrated that it has a good efficacy profile. However, it has a limited tolerability due to its antimuscarinic side effects. These effects are frequent with dose over 15 mg/day [23]. A maximum dose of 10 mg/day reached through progressive increase over a period of 3 weeks has been associated with lower incidence of side effects and maintaining effectiveness to treatment [24]. Dry mouth was the major side effect observed in several studies and was experienced by 70-100% of the patients treated with oxybutynin for primary or secondary hyperhidrosis. Other adverse effects include constipation and drowsiness, mild urinary retention, dry eyes, dizziness, diarrhea, mydriasis, and flushing were rare [25].

**II. CONCLUSION**

Based on the available evidences, topical glycopyrrolate, oxybutynin and botulinum toxin A should be considered as first-line therapies of facial hyperhidrosis due to their efficacy and safety.

**REFERENCES**


