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An Insight of Oxybutynin in Hyperhidrosis: Mechanism of Action and Efficacy; Review Article

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ABSTRACT

Background: For those with hyperhidrosis, the condition can cause psychological and social distress. Moreover, hyperhidrosis in certain sites as the palms can cause significant physical and occupational disability. Aluminum chloride, iontophoresis, sympathectomy botulinum toxin injections as well as oxybutynin have all been examined in the therapy of hyperhidrosis. As of yet, the perfect modality has not been discovered. In the absence of unambiguous data supporting one way over the other, selecting between multiple methods remains a clinical problem. In 1988, oxybutynin was linked to hyperhidrosis as an antimuscarinic medication. Individuals with primary severe hyperhidrosis or elderly patients who aren't eligible for surgery are increasingly turning to this medicine as an initial or alternate treatment.

Objective: Assessment of hyperhidrosis treatment effectiveness by oxybutynin and overview of its mechanism.

Methods: The databases were searched for articles published in English in 4 databases. PubMed, Google scholar, science direct, and Boolean operators (and or not) had been used such as oxybutynin chloride, hyperhidrosis, or hyperhidrosis treatment and in peer-reviewed articles between January 2005 and August 2021.

Conclusion: Oxybutynin chloride has been effectively used in the treatment of hyperhidrosis at different sites. It acts by inhibiting the muscarinic action of acetylcholine. Despite its satisfactory results, the treatment is associated with multiple side effects due to its anticholinergic action in the form of dry mouth, urinary retention, constipation, and headache. In addition, the majority of patients are unable to take it because of the lengthy daily administration schedule.

Keywords: Oxybutynin chloride, Hyperhidrosis.

INTRODUCTION

Excessive sweating can be caused by hyperhidrosis, a condition of the eccrine glands that results in unusually high sweating. An underlying illness such as an infectious, endocrine, or neurologic disorder can cause generalized hyperhidrosis. Idiopathic (primary) hyperhidrosis occurs in healthy individuals. It usually affects the palms, armpits, soles, or sometimes the face. Hyperhidrosis affects roughly 3% of the general population, primarily those aged 25 to 64 **(1).**

Focal hyperhidrosis may affect as many as 2.8% of the US population, according to current estimates. Most typically, it strikes adults between the ages of 25 and 64, but it can strike anyone, even as early as childhood. A hereditary propensity is found in 30–50 percent of those who have a family member who is sick **(2).**

The condition known as hyperhidrosis describes excessive sweating that isn't caused by heat or exertion. A lot of sweat can seep through your clothes or drip off your hands. Additionally, this form of excessive perspiration might create social anxiety and discomfort **(3):**

Prescription-strength antiperspirants are frequently the first step in treating hyperhidrosis. Try alternate drugs and therapy if antiperspirants don't work. Some doctors recommend surgery to remove sweat glands or disconnect nerves that cause an overproduction of sweat in extreme cases of hyperhidrosis **(4).**

Oxybutynin Chloride:

In the treatment of hyperhidrosis, oxybutynin, an anticholinergic medication, has emerged as an important option. It works for both localized and generalized hyperhidrosis, and patients of all ages, genders, and weights respond well to it. However, adverse effects can be severe enough in some patients that they must discontinue treatment. We should be looking forward to the development of an optimum protocol of administration with gradually rising dosage and data on long-term compliance to evaluate the long-term tolerance of the treatment **(5).**

Oxybutynin, commonly known as Ditropan XL, is an anticholinergic medicine approved by the FDA in 1975 for the treatment of overactive bladder symptoms. It has been extensively tested and proven to be safe and effective ever since. Patients with OAB can enjoy a better quality of life because of this medication. As a first-line treatment for OAB, it is frequently prescribed **(6).**

Indication:

Urinary incontinence and frequency can be alleviated with the use of oxybutynin, which is approved for the treatment of an overactive bladder. Oxybutynin can also be used to treat the symptoms of detrusor muscle overactivity, which has been linked to a neurological disorder, in children aged 6 and up. There are many conditions in which oxybutynin is used to treat urinary problems, including spina bifida. The off-label use of oxybutynin for the relief of ureteral

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stent or urinary catheter-related bladder spasm pain is not uncommon [7].

Oxybutynin's Mechanism of Action and Efficacy in Hyperhidrosis:

Hyperhidrosis was originally linked to the antimuscarinic effects of oxybutynin in 1988. Individuals with primary severe hyperhidrosis or elderly patients who aren't eligible for surgery are increasingly turning to this medicine as an initial or alternate treatment [8].

It has been shown that the molecule has a high safety profile in trials focusing on focal hyperhidrosis, such as the axillary, face, palmar, and plantar. Over 70% of the 50 patients studied in the first randomized, single-blinded, placebo-controlled trial in 2012 showed an improvement in symptoms when compared to placebo, which was a significant improvement. To begin with, patients received 2.5 mg twice daily for the first week, followed by 2.5 mg twice daily from days 8 through 21, then 5 mg twice daily beginning on day 22. For palmar, axillary, and plantar hyperhidrosis, the oxybutynin group showed a considerably better improvement than the placebo group. For individuals with palmar or axillary hyperhidrosis, the oxybutynin treatment group saw a significant improvement of more than 70%, but only 27.3 percent of the placebo group showed moderate improvement. More than 90% of those who received oxybutynin treatment for plantar hyperhidrotics improved somewhat or greatly, compared to only 13.4% of those who received a placebo [9].

A six-year follow-up study of 431 patients with axillary hyperhidrosis looked at the long-term effects of oxybutynin. The same dosage regimen was used. Fourteen patients were lost to follow-up on their first visit, and others didn't improve with oxybutynin after six weeks of treatment, so only 181 of the original 431 patients had their treatment monitored for more than six months [10].

The oxybutynin-treated 181 patients (129 females and 52 males) reported 93.4 percent improvement after six weeks and 82.9 percent continued to improve significantly after 24 weeks. Despite being referred for video-assisted thoracoscopic sympathectomy, 26 individuals showed good improvements with oxybutynin treatment after six weeks, even though they were unwilling to remain on long-term medication. A total of six individuals had to cease treatment because of adverse reactions. Comparing improvement levels after six weeks with those at the final evaluation (median of 17 months): the researchers found that 57.4 percent of patients had maintained their original improvement level, while 23.3% had improved further and 19.4 percent had reported degradation in the resolution of symptoms [11].

Anticholinergic side effects and the need for ongoing medication may limit oxybutynin's usage for some people with primary hyperhidrosis despite many trials showing its effectiveness. Symptoms such as urine retention, constipation, headache as well as dry mouth are more common when oxybutynin doses exceed 15 mg daily. For patients who are unable to tolerate the side effects of oxybutynin or who fail to recover after six weeks of treatment, sympathectomy or alternative treatment may be an option [12].

Tolerance for Risk as well as Safety:

When it comes to treating an overactive bladder, oxybutynin is a popular anticholinergic medicine. As a result, a wealth of knowledge on product safety and side effects has been amassed over many years. Closed-angle glaucoma is an absolute contraindication for the drug. Contraindications should also be considered in individuals with urinary retention, gastrointestinal retention, and documented allergy to the medicine or other components of the product [13].

The antimuscarinic side effects limit its tolerability. Aside from that, it is a safe agent. Doses above 15 mg/day are more likely to cause these side effects. According to research, an effective dose of 10 mg/day taken for three weeks has been shown to have fewer adverse effects and better compliance when administered in this manner. There have been numerous studies that have shown that starting with a dose of 1.25 mg and increasing it by 1.25 mg every four days up to a maximum dose of 7.5 mg/day, or starting with 2.5 mg/day, increasing it to 2.5 mg twice daily for the next two weeks, and finishing with 5 mg twice daily for the remainder of the treatment, works well [14].

In several investigations, dry mouth was the only complication that was reported. 70–100 percent of individuals treated with oxybutynin for hyperhidrosis suffer from dry mouth. Treatment with oxybutynin was rarely terminated due to dry mouth in studies lasting 6–12 weeks (1.56 percent) [15].

Hyperhidrosis and Oxybutin: Its Role in Treatment

The Canadian Hyperhidrosis Advisory Committee recommends the use of aluminum chloride as the first-line treatment for focal hyperhidrosis, according to their recommendations. Botulinum toxin injections and oral medicines are indicated as second- and third-line treatments for axillary hyperhidrosis, respectively. second-line therapy is iontophoresis, however, oxybutynin could also be considered because of its low cost and convenience as well as the growing research showing its reasonable efficacy and safety, as well as because of the greater cost of botulinum toxin injections. Oxybutynin should be the first-line treatment for craniofacial hyperhidrosis and primary extensive hyperhidrosis. Although it is not covered by insurance, the inexpensive cost of its use in the treatment of hyperhidrosis compensates for this feature. Without data on long-term usage of oxybutynin, we can't be sure that long-term adherence to therapy isn't going to be impaired by mouth dryness

that afflicts nearly all of the patients, even if it doesn't tend to get worse with time. In addition, the possibility of developing tachyphylaxis when using oxybutynin for an extended time is a cause for concern **(16).**

CONCLUSION

Oxybutynin chloride has been effectively used in the treatment of hyperhidrosis at different sites. It acts by inhibiting the muscarinic action of acetylcholine. Despite its satisfactory results, the treatment is associated with multiple side effects due to its anticholinergic action in the form of dry mouth, urinary retention, constipation, and headache. In addition, the majority of patients are unable to take it because of the lengthy daily administration schedule.

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REFERENCES

1. **Haider A, Solish N (2005):** Focal hyperhidrosis: diagnosis and management. CMAJ., 172(1): 1–7.
2. **Lynch O, Aherne T, Gibbons J *et al.* (2020):** Five-year follow-up of patients treated with intradermal botulinum toxin for axillary hyperhidrosis. Irish Journal of Medical Science, 189(3): 1023-1026.
3. **Alhetheli G (2021):** Outcome Using Either Intradermal Botox Injection or Endoscopic Thoracic Sympathectomy for Patients with Primary Palmar Hyperhidrosis: A Comparative Study. Cosmetics, 8(2): 41-47.
4. **Alsantali A (2018):** A comparative trial of ice application versus EMLA cream in the alleviation of pain during botulinum toxin injections for palmar hyperhidrosis. Clinical, Cosmetic and Investigational Dermatology, 11: 137-142.
5. **Lembrança L, Wolosker N, de Campos J *et al.* (2017):** Videothoracoscopic sympathectomy results after oxybutynin chloride treatment failure. Annals of Vascular Surgery, 43: 283-287.
6. **Kontochristopoulos G, Markantoni V, Agiasofitou E *et al.* (2021):** Treatment of primary axillary hyperhidrosis with a cream formulation of oxybutynin chloride 10%. Journal of the European Academy of Dermatology and Venereology, 35: 474–538.
7. **Campanati A, Gregoriou S, Consales V *et al.* (2020):** Combined treatment of palmar hyperhidrosis with botulinum toxin type A and oxybutynin chloride: Results of a clinical, multicenter, prospective study. Dermatologic Therapy, 20: 140-45.
8. **Thompson, S, Compton L (2021):** Pharmacologic Treatment of Antidepressant-Induced Excessive Sweating: A Systematic. Archives of Clinical Psychiatry (São Paulo), 48(1):57-65.
9. **Sammons J, Khachemoune A (2017):** Axillary hyperhidrosis: a focused review. Journal of Dermatological Treatment, 28(7): 582-590.
10. **Nawrocki S, Cha J (2019):** The etiology, diagnosis, and management of hyperhidrosis: a comprehensive review: therapeutic options. Journal of the American Academy of Dermatology, 81(3): 669-680.
11. **Gregoriou S, Sidiropoulou P, Kontochristopoulos G *et al.* (2019):** Management strategies of palmar hyperhidrosis: challenges and solutions. Clinical, Cosmetic and Investigational Dermatology, 12: 733-38.
12. **Wolosker N, Faustino C, de Campos J *et al.* (2020):** Comparative analysis of the results of videothoracoscopic sympathectomy in the treatment of hyperhidrosis in adolescent patients. Journal of Pediatric Surgery, 55(3): 418-424.
13. **Nguyen N, Gralla J, Abbott J *et al.* (2018):** Oxybutynin 3% gel for the treatment of primary focal hyperhidrosis in adolescents and young adults. Pediatric Dermatology, 35(2): 208-212.
14. **Hosp C, Hamm H (2017):** Safety of available and emerging drug therapies for hyperhidrosis. Expert Opinion on Drug Safety, 16(9): 1039-1049.
15. **García-Souto F, Del Boz J, Colmenero-Sendra M *et al.* (2020):** Craniofacial hyperhidrosis: Clinical characteristics and response to treatment in a cohort of 97 patients treated with oral oxybutynin. Dermatologic Therapy, 34: 1-10.
16. **Kuijpers M, Peeters G, Harms P *et al.* (2021):** Bilateral one-stage single-port sympathectomy in primary focal hyperhidrosis, a prospective cohort study: treat earlier?. Journal of Cardiothoracic Surgery, 16(1): 1-7.