



Letter to Editor

Treatment of Bromhidrosis with a 2% Glycopyrrolate Spray: A Retrospective Cohort Study

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Abstract

Background: Body odour, or bromhidrosis, is common and causes psychological distress. Current treatment options are limited in efficacy and severe side effects are not uncommon. Therefore, we formulated a topical spray containing glycopyrrolate 2%w/v to inhibit axillary apocrine and eccrine secretions, together with isopropyl alcohol and caprylyl glycol to reduce skin bacterial colonisation. **Objective:** To review the efficacy and safety of 2% glycopyrrolate spray in the treatment of bromhidrosis in patients who failed treatment with topical aluminium salts. **Methods:** In this retrospective cohort study, 18 patients aged 16-52 years old were included. The glycopyrrolate spray was applied to the axillae once to twice daily for 3 months and changes in a 5-point subjective bromhidrosis scale and the 4-point Hyperhidrosis Disease Severity Scale (HDSS) were evaluated. **Results:** The mean bromhidrosis score significantly improved from 2.72 (± 0.83) pre-treatment to 0.47 (± 0.61) post-treatment ($p < 0.001$). In patients with concurrent axillary hyperhidrosis ($n = 15$), the mean HDSS score improved from 2.73 (± 0.90) pre-treatment to 1.57 (± 0.65) post-treatment ($p < 0.01$). Side effects were minimal, with one patient reporting transient initial irritation. **Conclusion:** In our patient cohort with bromhidrosis with failed treatment with topical aluminium salts, topical glycopyrrolate 2%w/v spray effectively and safely reduced bromhidrosis and concurrent axillary hyperhidrosis.

Keywords: Odor; Anticholinergic; Glycopyrrolate; Osmidrosis; Hyperhidrosis; Sweat

Introduction

Body odour, or bromhidrosis, or osmidrosis, is common and causes psychological distress [1]. The primary mechanism of bromhidrosis is the degradation of skin apocrine secretions by commensal bacteria resulting in malodorous ammonia and short-chain fatty acids. This process most commonly occurs at the axillae [2]. Eccrine sweat secretion can additionally lead to skin

maceration, resulting in bacterial overgrowth and degradation of keratin, producing a foul smell [3].

Current treatment options are limited in efficacy and serious side effects are not uncommon. Non-pharmacological methods include antibacterial washes, topical agents that alter local pH, and antiperspirants containing aluminium salts that reduce sweating by temporarily plugging sweat ducts. These can cause irritant or allergic contact dermatitis or cyst formation due to chronic antiperspirant plugging of sweat glands and hair follicles [4,5]. Pharmacological treatments include topical or systemic antibiotic

therapy, which can lead to increased antimicrobial resistance. Moreover, these bacteria are commonly skin commensals and bromhidrosis may still recur after treatment. Oral anticholinergic drugs competitively inhibit acetylcholine at the muscarinic receptor, reducing sweat production, but can cause systemic anticholinergic side effects. Botulinum toxins, lasers and microwave treatment have been used, but are costly with variable results [2]. Surgical methods are typically reserved for refractory bromhidrosis, but can cause complications and scarring.

We thereby formulated a spray containing glycopyrrolate 2%w/v as the active ingredient to inhibit axillary apocrine secretion, together with isopropyl alcohol and caprylyl glycol to reduce skin bacterial colonisation and enhance active ingredient penetration. The aim of this retrospective study was to review the efficacy and safety of 2% glycopyrrolate spray in the treatment of bromhidrosis in a patient cohort who previously failed treatment with topical aluminium salts.

Methods

Patients seen at National Skin Centre Neurodermatology Clinic, Singapore, over three years from 2019-2022 were screened in this retrospective analysis. Patients with subjective reporting of bromhidrosis, with or without concomitant hyperhidrosis, who could not tolerate or had unsatisfactory results with topical aluminium salts and underwent treatment with 2% glycopyrrolate spray were included in this study.

The patients were instructed to use the glycopyrrolate spray once or twice daily for three months and then evaluated. The patients were assessed pre- and post- treatment using a 5-point bromhidrosis grading scale (Table 2). This in-house scale was devised as there is no established grading scale for bromhidrosis in literature. In addition, for patients with concurrent axillary hyperhidrosis, their severities were assessed using the Hyperhidrosis Disease Severity Scale (Table 2). These scales were used as convenient subjective assessment tools to reflect the extent to which bromhidrosis and axillary hyperhidrosis affected them psychosocially and therefore their need for therapy. The frequency of use needed for control of the condition, including any adverse events were recorded. Statistical analysis was performed using the Wilcoxon Signed-Rank Test and were carried out using SPSS version 24. The study was approved by the institution’s ethics committee.

Results

Eighteen patients aged between 16 and 52 years old with bromhidrosis were included in this study, of whom 11 (61.1%) were male. Among these 18 patients, 15 (83.3%) experienced concomitant axillary hyperhidrosis (Table 1). A summary of the patient characteristics is presented in Table 1.

Age, Mean (SD)	31.33 (11.82)
Gender, n(%)	
Male	11 (61.1%)
Race, n(%)	
Chinese	13 (72.2%)
Malay	1 (5.6%)
Indian	3 (16.7%)
Caucasian	1 (5.6%)
Condition, n(%)	
Bromhidrosis alone	3 (16.7%)
Bromhidrosis and axillary hyperhidrosis	15 (83.3%)
Frequency of spray used after 3-4 months, n(%)	
Less than once a day	2 (11.1%)
Once a day	13 (72.2%)
Twice a day	3 (16.7%)

Table 1: Patient Characteristics (n=18).

All 18 patients reported an improvement in scoring for their bromhidrosis, with a mean score of 2.72 (± 0.83) pre-treatment and 0.47 (± 0.61) post-treatment ($p < 0.001$). Of the 15 patients with concomitant axillary hyperhidrosis, 14 had a decrease in HDSS scoring, and the remaining one maintaining the same score. The mean score of hyperhidrosis pre-treatment was 2.73 (± 0.90) and the score post-treatment was 1.57 (± 0.65) ($p < 0.01$). These results are summarised in Table 2.

	Pre	Post	P-value ¹
Bromhidrosis Scale (0-4)²			
Mean (SD)	2.72 (.83)	.47 (.61)	p<0.001
Median (IQR)	2.5 (2, 3)	0 (0, 1)	
Hyperhidrosis Disease Severity Scale (1-4)^{3,4}			
Mean (SD)	2.73 (.90)	1.57 (.65)	p<0.01
Median (IQR)	2.5 (2, 4)	1.5 (1, 2)	

Table 2: Effects of Treatment on Bromhidrosis and Hyperhidrosis.

¹Wilcoxon Signed-Rank Test. ²5-point Bromhidrosis Scale where 0=not bothered, 1=little bothered, 2=somewhat bothered, 3=very bothered, 4=distressed. ³4-point Hyperhidrosis Disease Severity Scale (HDSS), where 1=My sweating is never noticeable and never interferes with my daily activities, 2=My sweating is tolerable but sometimes interferes with my daily activities, 3=My sweating is barely tolerable and frequently interferes with my daily activities, 4=My sweating is intolerable and always interferes with

my daily activities. ⁴Based on n=15 with Hyperhidrosis.

After three months, 13 out of the 18 patients (72.2%) were applying the spray once daily for symptom control, while three applied twice daily, and two applied the spray less frequently than once a day. Only one adverse event was reported, in which the patient complained of initial itchiness at the application site, but continued application without recurrence.

Discussion

Bromhidrosis is caused by bacterial degradation of apocrine secretions and is contributed by breakdown of keratin in a moist environment. Anticholinergics are an effective drug class that competitively inhibits acetylcholine at the muscarinic receptor, reducing sweat production from eccrine glands. A previous immunohistochemistry study did not identify muscarinic receptors on human apocrine glands [6]. However, similar to our study, a recent study by Gregoriou et al. found that glycopyrronium bromide 2% cream was effective in the treatment of bromhidrosis [7]. Patients with concurrent axillary hyperhidrosis in our study also experienced significant improvement. These findings suggest that a moist environment is important in the pathophysiology of bromhidrosis, or that apocrine glands do react to an anticholinergic agent.

The compounded formulation comprised glycopyrronium bromide as the active anticholinergic ingredient, and isopropyl alcohol and caprylyl glycol for antibacterial effect. Additionally, isopropyl alcohol rapidly evaporates to leave a dry skin surface and, together with caprylyl glycol, act as penetration enhancers for the active ingredient. The formulation also contains glycerin, a humectant which draws water to the corneocytes, to reduce possible skin barrier damage and irritation induced by isopropyl alcohol [8].

Instead of twice-daily use of the spray, 13 (72.2%) patients found that once-daily use was sufficient to control their symptoms for the whole day, and 2 patients (11.1%) only required a three-times-weekly frequency. The patients did not report systemic anticholinergic side effects, suggesting minimal systemic absorption of glycopyrronium bromide. Only one patient reported localised itch that was transient and resolved spontaneously. In contrast, mild to moderate irritation reported for aluminium salt-based topical antiperspirants was found to be more than 20% [5]. Therefore, topical glycopyrrolate can be a suitable alternative for patients who experience cutaneous side effects with topical antiperspirants.

There are numerous limitations in this study. Firstly, the study was not blinded and controlled. A randomised control trial will be required to definitively determine efficacy of such a spray. Secondly, the patients' scoring of their condition is subjective and can vary in relation to psychosocial factors, although there is currently no validated objective assessment for bromhidrosis. Thirdly, the follow-up evaluation of a subject's bromhidrosis and hyperhidrosis in this study was at only one time point. Nevertheless, the vast majority of patients in our Neurodermatology clinic are anecdotally still able to control their bromhidrosis well with the use of the topical glycopyrrolate spray after more than a year.

Conclusion

In our retrospective cohort of patients with bromhidrosis who failed therapy with topical aluminium salts, topical glycopyrrolate 2%w/v spray effectively and safely reduced bromhidrosis and concurrent axillary hyperhidrosis.

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