

# An Open-Label Trial of the Efficacy of 15% Aluminum Chloride in 2% Salicylic Acid Gel Base in the Treatment of Moderate-to-Severe Primary Axillary Hyperhidrosis

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## ABSTRACT

Primary focal hyperhidrosis (HH) is a chronic disorder of excessive sweating. A single-center, open-label study was performed to determine the efficacy and safety of 15% aluminum chloride (AC) in 2% salicylic acid gel base (SAGB) Hydrosal® in adults with moderate-to-severe primary axillary HH. Thirty subjects were given 15% AC in 2% SAGB to apply to their bilateral axillae nightly for the first week, then twice-weekly application as tolerated. The primary objective was change in mean Hyperhidrosis Disease Severity Score (HDSS) score from baseline to week 4. Participants who achieved an HDSS score  $\leq 2$  were designated as "responders." Mean change in HDSS from baseline to week 4 was 1.32 ( $p=0.0001$ ). At week 4, 21 of 29 (72%) were responders, and at week 12, 18 of 25 (72%) were responders. Based on these results, 15% AC in 2% SAGB may be an effective, high-strength AC topical therapy for treatment of patients with moderate-to-severe axillary HH.

## INTRODUCTION

Primary focal hyperhidrosis (HH) is a chronic, idiopathic disorder of excessive sweating in a bilateral, symmetrical manner. Excessive sweating affects nearly three percent of the United States (U.S.) population.<sup>1</sup> Approximately 1.4% of the U.S. population has axillary hyperhidrosis, with one-third having severe axillary hyperhidrosis (i.e., sweating that is barely tolerable and that frequently interferes with daily activities, or is intolerable and always interferes with daily activities).<sup>1</sup> First-line treatment consists of topical aluminum chloride therapy.<sup>2</sup> Over-the-counter (OTC) antiperspirants are often ineffective and prescription-strength formulations of 20% aluminum chloride (AC) in aqueous alcohol (AA) can be too irritating for patients to tolerate.<sup>3,4</sup> Iontophoresis, while an effective therapy for palmar and plantar hyperhidrosis, is not a practical treatment for axillary hyperhidrosis. Botulinum toxin type A is U.S. Food and Drug Administration (FDA)-approved for the treatment of moderate-to-severe axillary hyperhidrosis and is a very effective treatment for patients who fail or cannot tolerate therapy with topical aluminum chloride preparations and, in these patients, is considered second-line therapy.<sup>2,5</sup>

A recent study showed that 20% AC in a 4% salicylic acid gel base offered excellent efficacy and safety in the treatment of axillary HH, and was superior in efficacy and tolerability to 20% AC in AA.<sup>6</sup> This study was performed to determine the efficacy and safety of a different formulation of this topical antiperspirant with 15% AC in 2% salicylic acid gel base (SAGB) Hydrosal® in patients with moderate-to-severe primary axillary HH.

## MATERIALS AND METHODS

This study was a single-center, open-label study of patients with moderate-to-severe primary axillary HH as defined by a baseline score of 3 or 4 on the HDSS. The study duration was 12 weeks and was conducted at the Department of Dermatology at Saint Louis University. Patient recruitment began in June 2007 and ended in October 2007 with study completion in January 2008. The enrollment goal was 30 participants. The study duration was 12 weeks, beginning with the baseline visit at week 0 and concluding with the last follow-up visit at week 12. At the baseline visit, participants were screened for inclusion and exclusion criteria. This study was approved by the Saint Louis University Institutional Review Board.

Participants who met the inclusion criteria at the baseline visit were enrolled in the study after providing written informed consent form and a medical history, which included current medications and a physical exam. Participants were given 15% AC in 2% SAGB at the baseline visit and instructed to apply a

### TABLE 1.

#### Hyperhidrosis Disease Severity Scale

My underarm sweating is never noticeable and never interferes with my daily activities. (Score = 1)

My underarm sweating is tolerable but sometimes interferes with my daily activities. (Score = 2)

My underarm sweating is barely tolerable and frequently interferes with my daily activities. (Score = 3)

My underarm sweating is always noticeable and always interferes with my daily activities. (Score = 4)



thin layer of the gel (approximately a pea-sized amount per axilla) to the bilateral axillae nightly without occlusion for the first week, or as tolerated, and then wash the gel off the following morning. After the first week, participants were instructed to use the medication two times per week, or as tolerated or limited by irritation. At the baseline visit, participants completed the HDSS (Table 1) and the Hyperhidrosis Impact Questionnaire (HHIQ), two validated questionnaires which measure the impact and severity of hyperhidrosis. The validity and reliability of the HDSS have been analyzed using different studies and have been found to have strong-to-moderate correlations with the HHIQ, Dermatology Quality of Life Index (DLQI) and gravimetric sweat production measurements.<sup>4,7</sup> Subjects received follow-up telephone visits at weeks 1 and 8 to determine the HDSS score and to inquire about any adverse events or changes in medications. Participants returned for an outpatient follow-up visit at weeks 4 and 12 to assess for adverse events, changes in concomitant medications and to complete the HDSS, HHIQ and a third questionnaire, the Questions about Irritation (QI).

### Inclusion and Exclusion Criteria

Participants were male or female aged 12 years or older with moderate-to-severe primary axillary HH defined by a HDSS score of 3 or 4. No exclusions were made based on race or sex. Potential participants were excluded if they had received intradermal botulinum toxin type A injections for the treatment of axillary hyperhidrosis up to 6 months prior to enrollment; had allergy or any other contraindication to topical salicylic acid; had evidence of compromised axillary skin integrity due to a pre-existing skin condition; had used 20% AICI in aqueous alcohol up to 2 weeks prior to enrollment; or had taken an oral anti-

cholinergic up to 2 weeks prior to enrollment; had a sympathectomy of any type or surgical debulking of the sweat glands.

### Statistical Analysis

The primary objective was the frequency of response to treatment with 15% AC in SABG as measured by the mean change in HDSS score from baseline to week 4. Participants who achieved a score of HDSS  $\leq 2$  were designated as "responders." Secondary objectives included the mean changes in HDSS scores and the HDSS scores at weeks 1, 8 and 12. This study was designed to detect an  $\alpha = 0.05$  with 62% power based on an enrollment of 30 participants and assumed that 70% of patients would be "responders" by week 4 with an approximate 10% drop-out rate. All pair-wise statistical tests were two-sided and interpreted at a 5% significance level. Efficacy and safety analyses were conducted on an intent-to-treat basis. All subjects who received study medication were included in the analysis. The following demographic and baseline characteristics were evaluated: age, sex and baseline assessments based on the HDSS, HHIQ and QI questionnaires. For categorical baseline variables, a chi-square test was used; for continuous variables, a t-test was used to determine associations.

## RESULTS

Thirty patients were recruited and enrolled in the outpatient department of dermatology clinics at Saint Louis University and 29 (97%) completed through week 4; 25 (83.3%) completed through week 12. Three (10%) patients were lost to follow-up and two (6.6%) withdrew from the study due to intolerance of the medication. The majority of participants were female (87%) and the mean age was  $28.9 \pm 12.05$  years (Table 2). The mean HDSS score at baseline was  $3.32 \pm 0.476$ . Use of "normal strength" antiperspirants was reported by 66.7% of participants; 33% had used "high strength" antiperspirants. Specifically, seven par-

TABLE 2.

#### Demographic data

##### Gender

Females: 26 (87%)

Males: 4 (13%)

Mean age:  $28.9 \pm 12.05$  years

##### Prior high strength AC use

Yes: 13 (43%)

No: 17 (57%)

##### Baseline HDSS (subject-rated)

HDSS = 3: 20 (66.7%)

HDSS = 4: 10 (33.3%)

##### HDSS = hyperhidrosis disease severity scale

Mean baseline HDSS, all subjects:  $3.32 \pm 0.476$

Mean baseline HDSS, no prior high strength AC use:  
 $3.35 \pm 0.493$

Mean baseline HDSS, prior high strength AC use:  $3.31 \pm 0.480$

TABLE 3.

#### Adverse events at week 4

	Redness	Stinging	Itching	Fissuring	Pain
Mild or Absent	85.7%	71.5%	71.4%	100%	92.9%
Moderate	10.7%	17.9	17.9%	-	7.1%
Severe	3.6%	10.7%	10.7%	-	-

p < 0.5 compared with baseline

TABLE 4.

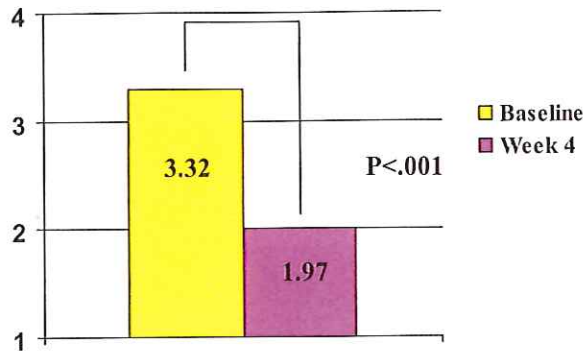
#### Adverse events at week 12

	Redness	Stinging	Itching	Fissuring	Pain
Absent or Mild	96%	92%	84%	100% (Absent)	94%
Moderate	4%	-	8%	-	6%
Severe	-	-	8%	-	-

p < 0.5 compared with week 4



**FIGURE 1.** Mean HDSS score decreased from 3.32 at baseline to 1.97 at Week 4 in subjects using 15% AC in 2% SAGB two to three times per week.



Participants (23.3%) had used 20% AC (Drysol™) and 3 (10%) had used 12% AC (Certain-Dri®). Eighty percent of subjects stated that treatment with previous antiperspirants was poor or ineffective and 83% were either somewhat or very dissatisfied with their current treatment for axillary HH.

#### Treatment Response and Change in Mean HDSS

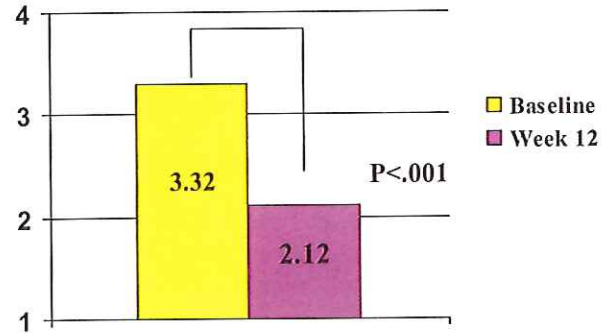
At weeks 1 and 4, 20 (66.7%) and 21 (72.4%) participants, respectively, were responders as measured by achievement of an HDSS  $\leq 2$ . At week 1, 30 participants reported a mean HDSS score of  $2.20 \pm 0.847$  ( $p < 0.001$ ), and at week 4 the mean HDSS reported by 29 subjects was  $1.97 \pm 0.778$  ( $p < 0.001$ ) (Figure 1). At week 8, 27 participants remained in the study and 19 (70.4%) were responders. At week 8, mean HDSS score was  $1.87 \pm 0.916$  ( $p = 0.0001$ ). By the end of the study at week 12, 25 participants remained and 18 (72%) were responders with a mean HDSS score of  $2.12 \pm 0.881$  ( $p < 0.001$ ) (Figure 2).

#### Treatment Response in Participants With Prior Use of High-Strength AC

Thirteen participants (43%) enrolled in the study had used either Drysol™, Certain-Dri® or both in the past. The mean HDSS score at baseline in this subgroup was  $3.31 \pm 0.480$ .

At week 1, the mean HDSS was  $2.08 \pm 0.95$  ( $p = 0.004$  vs. baseline), at week 4, the mean HDSS was  $2.00 \pm 0.91$  ( $p = 0.004$ ), at week 8, the mean HDSS was  $1.91 \pm 1.04$  ( $p = .011$ ), and at the study exit, the mean HDSS was  $2.20 \pm 1.14$  ( $p = 0.031$ ). At week 8, one participant withdrew due to intolerance of the medication and another participant was lost to follow up at this point, and, by study exit, one other participant had been lost to follow-up. The mean HDSS scores did not differ significantly from the group which had not used high-strength AC prior to study enrollment (Table 2). At week 1, 8 (69.2%) participants were responders; at week 4, 7 participants (61.5%) were responders. At weeks 8 and 12, 11 (72.7%) and 10 (70%) participants were responders.

**FIGURE 2.** Mean HDSS score decreased from 3.32 at baseline to 2.12 at Week 12 in subjects using 15% AC in 2% SAGB two to three times per week.



#### Satisfaction With Treatment With 15% AC in SAGB

Overall, participants reported significant improvements in satisfaction with treatment with 15% AC in SAGB. At week 4, 22 (75.8%) participants (75.8%) were either somewhat or very satisfied with their current treatment of their axillary HH compared with baseline ( $p < 0.001$ ). Similar results were observed at week 12, with 18 participants (75%) describing being somewhat or very satisfied with their current treatment compared with baseline ( $p < 0.001$ ). Regarding improvement in ability to perform current work activities, 20 participants (69%) reported being either somewhat or very satisfied compared with 23 participants (77%) who reported being somewhat or very dissatisfied ( $p < 0.001$ ) at week 4. This trend in improved performance of work activities continued at week 12 with 15 participants (62.5%) stating that they were either somewhat or very satisfied compared with baseline ( $p < 0.001$ ).

The subgroup that had used high-strength AC previously replied similarly, with eight participants (61.5%) stating that they were either somewhat or very satisfied with current treatment, and nine participants (69.2%) replying that they were either somewhat or very satisfied with their ability to perform their work activities. At study exit, the remaining eight participants in this subgroup reported comparable satisfaction.

#### Quality-of-Life Indices

Participants also experienced significant improvements in quality-of-life indices assayed by the HHIQ. Specifically, participants reported significant improvements in frequency of changing shirts during the day, improved emotional status regarding their hyperhidrosis, improvements in multiple activities or social situations, and improved effectiveness at work.

#### Adverse Events

##### Questions About Irritation

All participants completed a questionnaire, QI at baseline,



weeks 4 and 12 regarding symptoms of axillary irritation. Two participants (6.7%) did not complete the study due to moderate-to-severe axillary irritation (described as redness, itching and burning) related to use of 15% AC in 2% SAGB. Both of these patients had reported previous use and significant intolerance of 20% AC in AA in the past. The majority of participants at weeks 4 and 12 reported absent-to-mild symptoms of irritation such as redness, stinging, itching or fissuring (Tables 3 and 4). The only significant complaint at week 4 was associated with stinging, which eight participants (26.7%) described as moderate or severe ( $p=0.012$ ), but which had improved significantly by week 12 ( $p=0.022$ ). Participants did not complain of any other side effects or adverse events from use of 15% AC in 2% SAGB.

### DISCUSSION

This open-label pilot study of the efficacy and safety of 15% AC in 2% SAGB demonstrated improvement in over 70% of participants with moderate-to-severe axillary hyperhidrosis and was well-tolerated with minimal side effects. This medication was successful in treating patients who had previously failed other high-strength aluminum chloride medications, with nearly 70% of these participants achieving significant improvement in HDSS scores. However, in this small study, 7% of participants were unable to tolerate the medication due to excessive irritation, and both of these patients had reported poorly tolerating high-strength aluminum chloride in the past. The majority of participants expressed satisfaction with treatment and experienced improvements in numerous indices of quality of life.

### CONCLUSION

Therefore, this small pilot study showed that 15% AC in 2% SAGB may be an effective alternative high strength aluminum chloride topical therapy for first-line treatment of patients with moderate-to-severe axillary hyperhidrosis, and may benefit patients who have failed other high strength aluminum chloride medications previously.

### DISCLOSURES

The authors have no conflicts of interest to disclose.

### ACKNOWLEDGEMENTS

Valeo Pharma provided financial support through an unrestricted educational grant. The sponsor had no role in the analysis or interpretation of the results of this research. No limitations on publication were imposed, and review before final publication was not required. The authors made final decisions on all aspects of the manuscript.

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