

A Pilot Study on Polidocanol Injection as Treatment for Primary Axillary Hyperhidrosis

Keywords: Polidocanol; Axillary hyperhidrosis

Abstract

Background: Hyperhidrosis is a condition marked by excessive sweating that can be debilitating leading to emotional and social embarrassment, as well as occupational, physical and psychological disability. Currently, treatment options available include pharmacologic and surgical. Pharmacologic treatments include topical aluminum salts, iontophoresis, systemic medications and botulinum toxin injection. Meanwhile, surgical treatments include liposuction, direct excision of the glands, sympathectomy and laser treatment. The aforementioned treatments provide only temporary results, may have disabling side effects, may be expensive and some are more invasive that may lead to complications. There are a few studies regarding the use of sclerotherapy for chemical ablation of the sweat glands to treat axillary osmidrosis but, none yet for polidocanol and for axillary hyperhidrosis.

Objective: The study aimed to determine the efficacy and safety of polidocanol injection as treatment for primary axillary hyperhidrosis.

Methods: Patients with primary axillary hyperhidrosis were enrolled. Identified hyperhidrotic areas were determined and injected with 1% polidocanol. The degree of hyperhidrosis was assessed using Hyperhidrosis Disease Severity Scale (HDSS), and Sweating Intensity Visual Scale (SIVS) at baseline, 2 and 4 weeks after injection.

Results: There was percentage reduction in sweating as reflected in the HDSS and SIVS scores pre-treatment and post treatment. The highest mean difference was noted between baseline and week 4. Results showed improvement of hyperhidrosis. However due to the limited number of patients, data was not all statistically significant. Patients reported slight discomfort after the procedure but it immediately waned. No other adverse events were noted.

Conclusion: Polidocanol 1% injection may be a promising treatment modality for primary axillary hyperhidrosis. It is effective and safe, and also inexpensive, less invasive and with minimal complications compared to ethanol and surgery.

Introduction

Hyperhidrosis is a condition marked by excessive sweating. It is a chronic autonomic disorder that can be debilitating leading to emotional and social embarrassment, as well as occupational, physical and psychological disability [1]. According to standardized and validated quality-of-life surveys, the negative effects of hyperhidrosis are comparable to other conditions, such as severe psoriasis, end-stage renal disease, rheumatoid arthritis, and multiple sclerosis [2]. In 2004, Hornberger, et al [3] defined primary focal hyperhidrosis as excessive [3], bilateral, and relatively symmetric sweating occurring in at least one of the following sites: the axillae, palms, soles, or craniofacial region. The following criteria are recommended for diagnosing primary focal hyperhidrosis: focal, visible, excessive sweating of at least 6 months duration without apparent cause with at least two of the following characteristics: a) bilateral and relatively symmetric; b) impairs daily activities; c) frequency of at least one episode per week;

Open Access

Research Article



Journal of Clinical & Investigative Dermatology

Calayan-Terte CMY¹, Espinoza-Thaebtharm A² and Lopez-Villafuerte L²

Department of Dermatology, Jose R. Reyes Memorial Medical Center, Philippines

*Address for Correspondence

Calayan-Terte CMY, Department of Dermatology, Jose R. Reyes Memorial Medical Center, Manila, Philippines, Tel: 63-917 560 8391; E-mail: kimee_calayan@yahoo.com

Submission: 13 February, 2020

Accepted: 24 March, 2020

Published: 26 March, 2020

Copyright: © 2020 Calayan-Terte CMY, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

d) age of onset less than 25 years; e) positive family history and f) cessation of focal sweating during sleep [4]. Secondary hyperhidrosis on the other hand, can be drug-induced, toxin-induced, caused by a systemic illness, by congenital disorders or it can be compensatory [5].

Currently, treatment options available include pharmacologic and surgical. Pharmacologic treatments include topical aluminum salts, iontophoresis, systemic medications (i.e. glycopyrrolate, menthatheline bromide, oxybutynin and clonidine) and botulinum toxin injection. Meanwhile, surgical treatments include liposuction, direct excision of the glands, sympathectomy [4] and laser treatment. The limitations of the aforementioned treatments are: a) provide only temporary results; b) have disabling side effects; c) may be expensive; and d) some are more invasive that may lead to complications.

Sclerotherapy is the use of physical, chemical, and biological properties of an agent used to disrupt target tissue. Sclerosants induce inflammatory response that result to fibrosis, thrombosis, extraction of proteins from lipids, denaturation of proteins, cell dehydration by osmosis, and physical obstruction by polymerization. The result of these processes is controlled disruption of the targeted tissues' biologic function [6]. Sclerosing solutions include ethanol, hypertonic saline, sodium tetradecyl sulfate, polidocanol, sodium morrhuate, polyiodide iodide and glycerin [6,7]. In dermatology, sclerotherapy is commonly indicated for the treatment of insufficient veins, recurrent varicosities and venous malformations [8].

In our literature search, there are only a few studies regarding the use of sclerotherapy, specifically ethanol, for chemical ablation of the sweat glands to treat axillary osmidrosis [10,11] but, none yet for polidocanol and for axillary hyperhidrosis. Hence, this study aims to investigate the use of polidocanol as a novel therapeutic option in providing a permanent, cost-effective and less invasive method in treating primary axillary hyperhidrosis.


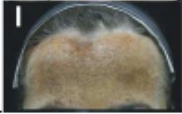

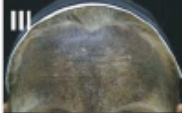


Methodology

Study design and study population

Table 1: Hyperhidrosis Disease Severity Scale (HDSS) [15].

Condition	Score
My axillary sweating is never noticeable and never interferes with my daily activities	1
My axillary sweating is tolerable but sometimes interferes with my daily activities	2
My axillary sweating is barely tolerable and frequently interferes with my daily activities	3
My axillary sweating is intolerable and always interferes with my daily activities	4

Table 2: Sweating Intensity Visual Scale (SIVS) [13].

Sweating Intensity	Grade
0 	0
I 	I
II 	II
III 	III
IV 	IV
V 	V

This study is a non-blinded, non-randomized, controlled pilot study conducted at the Jose R. Reyes Memorial Medical Center Department of Dermatology. The Institutional Review Board of this institution approved the study following the guidelines of good clinical practice.

Patients aged 18 to 40 years old, male and female, who tested positive in the Minor’s iodine starch test and with moderate to severe hyperhidrosis with a score of 3 or 4 in the Hyperhidrosis Disease Severity Score (HDSS) (Table 1), were included in the study.

Patients who were pregnant or breast-feeding, have secondary hyperhidrosis, infections or dermatoses over the axillae, neuromuscular diseases, taking systemic medications that could interfere with neuromuscular activity and who tested negative in the Minor’s iodine starch test were excluded. Patients who were using anti-perspirant were instructed to discontinue its use for a week prior

and throughout the duration of the study.

Study intervention and outcome assessment

The nature and purpose of this study were explained to potential participants. Six eligible patients were recruited and a comprehensive written informed consent was obtained. Detailed history was taken and participants were screened by having them answer the HDSS and undergoing the Minor’s iodine starch test. The Minor’s iodine starch test was performed by the primary author by spreading 10% iodine solution on the axillae, and then corn starch powder was applied after. After 15 minutes or so, in room temperature of 30-35 °C, the presence of sweating was indicated by the onset of a dark-blue color [9] on the participants’ axillae. The Minor’s iodine starch test was evaluated using the Sweating Intensity Visual Scale (SIVS) (Table 2).

The intervention was performed by the primary author under the supervision of the co-authors. Patients were placed in a supine

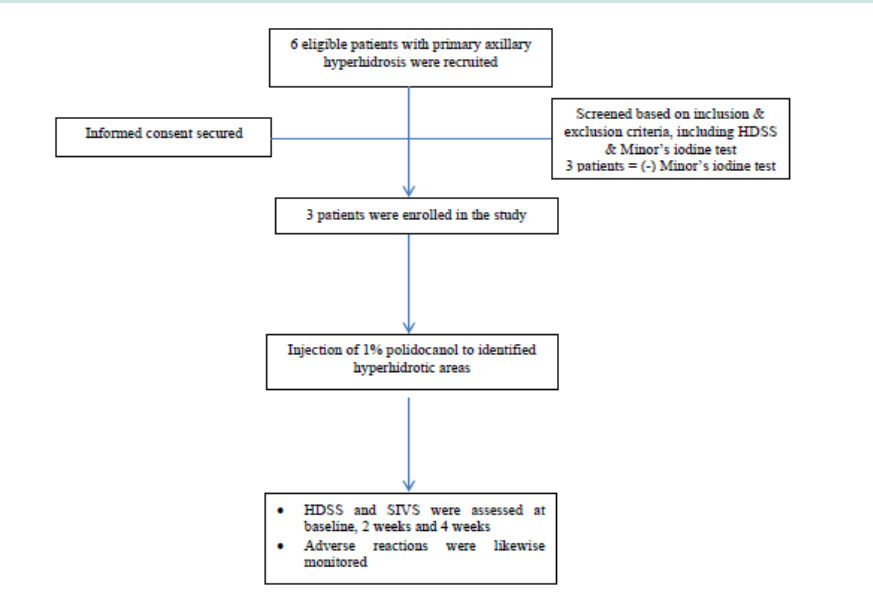


Figure 1: Schematic diagram of methodology.

Table 3: Percentage of reduction of SIVS scores between pre-treatment and post treatment.

Patient No.	Percentage of Reduction			Remarks
	Baseline	Week 2	Week 4	
1	2	0(100%)	0(100.0%)	Minimal or no sweating
2	3	2(33.3%)	1(66.7%)	Initial, discrete sweating
3	2	1(50.0%)	0(100%)	Minimal or no sweating

Table 4: Percentage of reduction of HDSS scores between pre-treatment and post treatment.

Patient No.	Percentage of Reduction			Remarks
	Baseline	Week 2	Week 4	
1	3	2(33.3%)	2(33.3%)	Mild to moderate hyperhidrosis
2	4	2(50.0%)	2(50.0%)	Mild to moderate hyperhidrosis
3	4	2(50.0%)	2(50.0%)	Mild to moderate hyperhidrosis

position with their arms abducted to expose the axilla. The identified hyperhidrotic areas from the Minor's starch iodine test were marked with a dermatographic pen and each area was divided into 1 cm² squares. The treatment areas were cleaned using gauze soaked in sterile water. A dose of 0.1 ml of 1% polidocanol was then injected subdermally into each square using a tuberculin syringe with a gauge 30 needle. A total of 2 ml on the average was injected. Documentation through photography was done at baseline and at specified follow-up periods.

Follow-up periods were at 2 weeks and 4 weeks after 1% polidocanol injection to assess its efficacy in reducing hyperhidrosis. The degree of hyperhidrosis were determined by 3 study associates (primary author's co-residents) using the SIVS at baseline, 2 weeks and 4 weeks. Patients answered the HDSS during follow-up visits as well. Adverse events, such as allergic reaction, pigmentation and skin necrosis, were also monitored.

Statistical analysis: For the descriptive analysis, means with their corresponding standard deviations were used to describe the demographic characteristics of the participants, which include age, gender and duration of hyperhidrosis. For the HDSS and SIVS pre-

treatment and post-treatment scores, percentage of reduction was computed. For the inferential statistics, Kruskal-Wallis is test with its associated p-value of <0.05 was used to determine if the difference between the SIVS and HDSS pre-treatment and post-treatment scores were statistically significant (Figure 1)

Results

A total of 3 patients were enrolled in the study. There were 2 females and 1 male with an average age of 31.67 (age range between 23 to 38 years; SD = ±7.77). The Mean ± SD duration of the axillary hyperhidrosis was 8.33 ± 1.53 years. Table 3 shows the comparison of SIVS scores between pre-treatment and post treatment in terms of percentage of reduction. For patient 1, it was observed with a 100% reduction at week 2 until week 4. Patient 2 also showed 33.3% reduction at week 2 and remarkable percentage reduction of 66.7% at week 4. Patient 3 on the other hand had 50% reduction at week 2 and 100% reduction at week 4. The results implied that there was already a reduction in sweating at a 2-week observation schedule. At the end of 4 weeks, SIVS scores showed initial, discrete sweating to minimal or no sweating.

Table 5: Kruskal-Wallis analysis of SIVS and HDSS scores between pre-treatment and post treatment.

Scale	Duration	Mean Rank	χ^2 -value	p-value $p = 0.05$	Remarks
SIVS	Baseline	7.67	5.213	0.074	Not Significant
	Week 2	4.50			
	Week 4	2.83			
HDSS	Baseline	8	7.714	0.021	Significant
	Week 2	3.50			
	Week 4	3.50			

In Table 4, comparison of HDSS scores based on percentage of reduction is shown. The HDSS baseline scores of patients 1, 2 and 3 were 3, 4 and 4 respectively. The scores of 3 or 4 indicate severe hyperhidrosis. Patient 1 had 33.3% reduction at week 2 and continuously at week 4. Moreover, highest reduction percentage was observed in Patient 2 and 3. Patient 2 and 3 gathered 50% reduction rate at week 2 and continuously at week 4. The HDSS grading scores of the three patients is equal to 2 after 4 weeks of treatment. A score of 1 or 2 indicates mild or moderate hyperhidrosis.

The patients' SIVS and HDSS scores were assessed using Kruskal-Wallis test and the results are summarized in Table 5. The SIVS χ^2 - value was 5.213 while the p-value was 0.074. With p-value more than 0.05, there was no significant difference on the SIVS scores between pre-treatment and post treatment. In contrast, the HDSS χ^2 - value and p-value were 7.714 and 0.021, respectively. With p-value less than 0.05, there was a significant difference on HDSS scores between pre-treatment and post treatment.

Results showed that using 1% polidocanol improved primary axillary hyperhidrosis as reflected in the percentage reduction in SIVS and HDSS scores, though not statistically significant for SIVS.

Patients reported slight discomfort after the procedure but it immediately waned. Allergic reaction, pigmentation and skin necrosis were monitored and recorded. No adverse reactions were observed in all patients.

Discussion

There are numerous treatment modalities for primary axillary hyperhidrosis however, not all patients get satisfied with the results. Removal of the sweat glands offers a permanent solution to the problem. Various techniques in literature have been used to achieve this, such as direct surgical excision and liposuction. Although the success rate of these surgical approaches is high, wound complications and unsightly scarring are major concerns. In addition, patients require a long postoperative immobilization and recovery time [10]. Moreover, the trend in cosmetic medicine is towards use of noninvasive techniques, but effectiveness and durability are also important. Patients prefer a shorter recovery time, especially with cosmetic procedures or treatment of benign conditions [10]. Chemical ablation of the sweat glands using sclerotherapy provides an alternative approach to surgery. In a study by Hyung-Sup et al [11] sclerotherapy using absolute ethanol combined with minimal subdermal shaving was done to treat axillary osmidrosis. Results showed decrease in malodor and minimal complications, and patients were satisfied with the outcomes until six months after. Another study by Han and Li [10] percutaneous ethanol injection for chemical ablation of sweat glands was used to treat axillary osmidrosis. Majority of patients (92.1%) considered themselves satisfied with

their results. The proposed mechanism of this technique is that when ethanol is injected into the subcutaneous layer near the interface of the dermis, where the apocrine and eccrine glands are located, it will cause necrosis of the glands, while the superficial skin and underlying vital structures are left intact. However, skin necrosis still developed in some of the patients [10]. Compared to ethanol, polidocanol has a better safety profile. It is painless upon injection, does not produce tissue necrosis if extra vasated, and has a very low incidence of allergic reactions, although a few cases of anaphylaxis have been reported [12]. In this study, injection of 1% polidocanol for chemical ablation of sweat glands, preliminary results showed a significant reduction of sweating as reflected in both SIVS and HDSS scores, though not yet statistically significant for SIVS. Moreover, dreaded complications such as skin necrosis did not develop.

Conclusion and Recommendations

Polidocanol 1% injection may be a promising treatment modality for primary axillary hyperhidrosis. It is effective and safe, and also inexpensive, simpler, less invasive and with minimal complications compared to ethanol and surgery. The authors recommend a larger sample size because a small number of cases limit statistical analysis. A longer follow-up period is also recommended to document long-term effects and for any recurrence. If feasible, a biopsy may be done to confirm destruction of sweat glands.

References

- Naumann MK, Hamm H, Lowe NJ (2002) Effect of botulinum toxin type a on quality of life measures in patients with excessive axillary sweating: a randomized controlled trial. Br J Dermatol 147: 1218-1226.
- Cina CS, Clase CM (1999) The Illness Intrusiveness Rating Scale: a measure of severity in individuals with hyperhidrosis. Qual Life Res 8: 693-698.
- Hornberger J, Grimes K, Naumann M, Glaser DA, Lowe NJ, et al. (2004) Recognition, diagnosis, and treatment of primary focal hyperhidrosis. J AmAcadDermatol 51: 274-286.
- Amanda-Amrita D, LakrajJabbari B (2013) Hyperhidrosis: Anatomy, Pathophysiology and Treatment with Emphasis on the Role of Botulinum Toxins. Toxins (Basel) 5: 821-840.
- Fujimoto T, Kawahara K, Yokozeki H (2013) Epidemiological study and considerations of primary focal hyperhidrosis in Japan: From questionnaire analysis. J Dermatol40: 886-890.
- Albanese G, Kondo KL (2010) Pharmacology of sclerotherapy. Semin Intervent Radiol 27: 391-399.
- Goldman M, Weiss R (2012) Phlebology and treatment of leg veins. In: Bologna J, Jorizzo J, Schaffer J, eds. Dermatology (3rd edn). USA: Elsevier 2509-2523.
- Lorenz MB, Gkogkolou P, Goerge T (2014) Sclerotherapy of varicose veins in dermatology. J Dtsch Dermatol Ges 391-393.
- D'Epiro S, Macaluso L, Salvi M, Luci C, Mattozzi C, et al. (2014) Safety and prolonged efficacy of Botulin Toxin A in primary hyperhidrosis. Clin Ter 165: e395-400.

ISSN: 2373-1044

10. Han X, Li F (2013) Percutaneous ethanol injection for the treatment of axillary osmidrosis. *Clin Exp Dermatol* 38: 484-488.
11. Hyung-Sup S, Sung-Kee M, Jins-Soo L, Ki-Taik H, Min-Cheol K (2013) Minimal subdermal shaving by means of sclerotherapy using absolute ethanol: a new method. *Arch Plast Surg* 40: 440-444.
12. Feied CF (2007) Sclerosing Solutions. In: Fronek H (ed). *The Fundamentals of Phlebology, Venous Disease for Clinicians* 2nd American College of Phlebology 23.
13. Hexsel D, Rodrigues T, Soirefmann M, Zechmeidter-Prado D (2010) Recommendations for performing and evaluating the results of the minor test according to a Sweating Intensity Visual Scale. *Dermatol Surg* 36: 120-122.
14. Swineheart JM (2000) Treatment of axillary hyperhidrosis: combination of the starch-iodine test with the tumescent liposuction technique. *Dermatol Surg* 26: 392-396.
15. Hyperhidrosis disease severity scale. International Hyperhidrosis Society.