Successful Treatment of Axillary Hyperhidrosis With Aluminum Chloride Hexahydrate 15% in Salicylic Acid 2% Gel

Antranik Benohanian, MD

Axillary hyperhidrosis (HH) has been a neglected subject in medical literature. In the past few decades, aluminum chloride hexahydrate 20% in absolute alcohol was the main approach to treat this condition. Failure to respond to this modality would often be an indication for the surgical removal of the axillary sweat glands. This report describes a case of axillary hyperhidrosis who after failing to respond to aluminum chloride hexahydrate 20% in an alcohol vehicle, responded favorably well to aluminum chloride hexahydrate 15% in a salicylic acid 2% gel formulation.

Focal hyperhidrosis (HH) involves mainly the axillae, the hands and feet, and, less frequently, the face, the groin, and the craniofacial and inframammary areas, among others. Adar et al[1] reported an incidence of HH of 0.6% to 1% for all severities and locations. Disturbing focal HH affects at least 2.8% of the US population (8.5 million people). Only 38% of affected individuals had discussed their sweating with a health care professional. Approximately half of these individuals suffer from axillary HH.[2] The hands and feet are affected in approximately 60% of patients, alone or in combination with other sites.[3] The highest prevalence ever reported for palmar HH was 4.36%, among Chinese adolescents.[4] Many believe that the true figures are much higher because available statistics do not include individuals who only sweat moderately or in certain situations and who do not seek professional help.

Dr. Benohanian is Dermatologist, Montreal University Hospital Center, Canada.

Dr. Benohanian is consultant for Allergan, Inc, and Valeo Pharma, Inc.

Correspondence : Antranik Benohanian, MD, 552 Emile-Journault, Montreal, QC, H2M 1J7, Canada (info@benohanian.com).

During the past few decades, the standard topical application used to treat focal HH has been aluminum chloride hexahydrate 6.5% to 20% in absolute alcohol. Failure to respond to that modality would be an indication for surgery. Botulinum toxin type A (BTX-A) injections have revolutionized the treatment of focal HH, and surgery is rarely performed nowadays. BTX-A was approved for severe axillary HH unresponsive to topical applications by Health Canada in August 2001 and by the US Food and Drug Administration in July 2004. Unfortunately, treatment with BTX-A is not affordable to everyone, and many patients still consider the surgical option to achieve permanent relief.

This case report illustrates the benefit of using aluminum chloride hexahydrate, formulated in aluminum chloride hexahydrate 15% with salicylic acid (SA) 2% in a gel vehicle, in lieu of the conventional aluminum chloride hexahydrate 20% in absolute alcohol, to treat axillary HH.

CASE REPORT

A 37-year-old female patient, suffering from disabling axillary HH since her adolescence, consulted for surgery after failing to respond to aluminum chloride hexahydrate in absolute alcohol. Her mother had also suffered

from the same problem at a younger age. The patient's HH had negatively impacted her quality of life because she had to change her clothing 3 to 4 times a day due to visible sweat stains that caused an unjustifiable rise in the cost of laundering and replacing damaged clothing.

Treatment with BTX-A was considered, but the patient declined that option because she did not possess a health insurance plan that would cover the cost. The surgical option was also turned down because the patient was concerned that disfiguring scars would remain after the removal of the axillary glands.

The patient had been treated with nightly applications of aluminum chloride hexahydrate 15% in SA 2% gel for a week, to which she responded positively; later, she gradually reduced the frequency to once or twice a week.

COMMENT

In 1916, Stillians[5] first introduced aluminum chloride hexahydrate in an aqueous solution. Although effective, irritation of the skin and damage to clothing were major disadvantages of this formulation. Irritation is due to the formation of hydrochloric acid that results from the reaction of aluminum chloride hexahydrate with water. Later, absolute alcohol was suggested as the best vehicle for minimizing irritation caused by aluminum chloride hexahydrate, and many clinicians still use this particular vehicle.

In February 1978, a middle-aged female patient suffering from axillary HH requested from me a stronger formulation than the classic aluminum chloride hexahydrate 20% solution, to which she failed to respond even under occlusion. Because aluminum chloride hexahydrate has the strongest drying property among the ingredients used in antiperspirants, it was combined with SA in order to potentiate its antiperspirant effect, since SA is also known for its antiperspirant properties. At the time, a hydroalcoholic gel containing SA 5% was available on the market as an antiacne preparation. Many dermatologists used the hydroalcoholic gel containing SA 5% to treat acne in adolescents, and some went even further by adding aluminum chloride hexahydrate 6% to the gel to obtain an accrued antiacne effect. I prescribed aluminum chloride hexahydrate 20% in a hydroalcoholic gel containing SA 5%, which, at the end of preparation, contained SA 4%. I also warned the patient that a severe irritation might occur because of the presence of aluminum chloride hexahydrate and SA, and if so, a hydrocortisone 1% cream should be applied after thoroughly washing the treated area. To my greatest surprise, an ecstatic patient called me the following day to inform me that not only had the formulation worked, but it was also better tolerated. Her surgery was cancelled and more than 100 similar cases were referred to me during that same year by the surgeon who originally planned her surgery.[6] This was my first use of aluminum chloride hexahydrate 20% in SA 4%. This unexpected successful outcome radically changed my approach to treating focal HH, and since then I have used aluminum chloride hexahydrate at concentrations varying from 10% to 55%, always in a gel vehicle, with or without the association of SA 2% to 6% as an enhancer,[7,8] depending on the age of the patient, the area involved, the severity of the disease, and the patient's own tolerance of previous medications. The most common concentration used as a first line treatment for focal HH in general was aluminum chloride hexahydrate 15% in SA 2% gel. My latest step-up approaches for the treatment of axillary and palmoplantar HH are indicated in Tables 1 and 2, respectively.

Recently, aluminum chloride hexahydrate 15% in SA 2% gel became available in Canada and the United States. The preparation could also be used as a gel base in order to obtain higher concentrations of aluminum chloride hexahydrate, to which SA could also be added as an enhancer.

After successfully treating hundreds of patients with the gel formulation, there was no doubt in my mind that a gel vehicle would be more effective and better tolerated than an alcohol solution. Evidence to corroborate this fact did not come until many years later.[9,10] In 2002, Hölzle[11] finally confirmed that an aqueous vehicle thickened with methylcellulose to create a gel was the most effective

Table 1

The Order of Step-up Approaches for the Treatment of Axillary Hyperhidrosis

Over-the-counter antiperspirants
Aluminum chloride hexahydrate 15% in SA 2% gel
Aluminum chloride hexahydrate 15% in SA 2% gel compounded to aluminum chloride hexahydrate 20%–30% and SA 4%
BTX-A 50 U per axilla or groin
Aluminum chloride hexahydrate 15% in SA 2% gel to prolong interinjection interval if necessary
BTX-A 100 U per axilla or groin
Aluminum chloride hexahydrate 15% in SA 2% gel + anticholinergic if necessary
Surgery: excision of axillary glands if not associated with palmar HH; endoscopic thoracic surgery if associated with palmar HH

Abbreviations: SA, salicylic acid; BTX-A, botulinum toxin type A; HH, hyperhidrosis.

TABLE 2

Step-up Approaches for the Treatment of Palmoplantar Hyperhidrosis

Aluminum chloride hexahydrate 15% in SA 2% gel
Aluminum chloride hexahydrate 15% in SA 2% gel compounded to aluminum chloride hexahydrate 30%–40% and SA 4%
Aluminum chloride hexahydrate 15% in SA 2% gel compounded to aluminum chloride hexahydrate 55% and SA 6%
Iontophoresis + aluminum chloride hexahydrate 15% in SA 2% gel compounded to aluminum chloride hexahydrate 15%–55% and SA 2%–6% + anticholinergic if necessary
BTX-A 100 U per palm or 150 per foot + aluminum chloride hexahydrate 15% in SA 2% gel compounded to aluminum chloride hexahydrate 15%–55% and SA 2%–6% + anticholinergic if necessary
BTX-A 150–200 U per palm or 200–250 U per foot + aluminum chloride hexahydrate 15% in SA 2% gel compounded to aluminum chloride hexahydrate 15%–55% and SA 2%–6% + anticholinergic if necessary
Endoscopic thoracic sympathectomy for palmar HH or endoscopic thoracic sympathectomy for plantar HH

Abbreviations: SA, salicylic acid; BTX-A, botulinum toxin type A; HH, hyperhidrosis.

formulation to enhance the efficacy and reduce the irritation caused by aluminum chloride hexahydrate in a large series of patients followed for as long as a decade.

In a gel vehicle, with or without SA as an enhancer, aluminum chloride hexahydrate offers several advantages in the treatment of focal HH. It may be used as a first line therapy in focal HH because, as mentioned previously, a gel vehicle is more effective and better tolerated than an alcohol solution. The aluminum chloride hexahydrate molecule in a gel vehicle remains firmly fixed at the treatment site, whereas an alcohol solution may carry it away.

The rationale behind adding SA in a gel vehicle is that it may enhance the penetration of aluminum chloride hexahydrate through the thick, horny layer of skin present on the hands and feet.[12] Of all the skin covering the body, none is tougher or thicker than that covering the palms and soles, which renders the treatment of HH in these areas a therapeutic challenge. The SA also acts synergistically with aluminum chloride hexahydrate to enhance its antiperspirant effect, since SA has antiperspirant properties of its own.[13]

Moreover, although aluminum chloride hexahydrate is soluble in a ratio of 1:1 in water, it is only soluble in a ratio of 1:4 in ethanol. That means that aluminum chloride hexahydrate in an alcohol solution cannot be raised easily beyond 25%, whereas in an aqueous or hydroalcoholic vehicle, thickened with a cellulose polymer to create a gel, aluminum chloride hexahydrate is dispersed in the form of microcrystals that allow aluminum chloride hexahydrate to reach supersaturated concentrations well above 40% and up to 55%.[14,15]

Hölzle and Braun-Falco[16] also reported that long-term blockage of the distal acrosyringium due to aluminum salts may lead to functional and structural degeneration of the eccrine acini, thereby considerably reducing the amount of sweating. That explains why some patients stop sweating after a certain number of months or years.

The aluminum chloride hexahydrate may be used as an adjunct treatment to iontophoresis or BTX-A when these treatments alone fail to control focal HH. This is of the utmost importance in cases of palmar and plantar HH because these sites require a much higher dose of BTX-A than the axillae (ie, 100–200 U per palm or 150–250 U per sole to control HH).[8] Another difficulty facing the clinician willing to treat palmar and plantar HH with BTX-A is the intense pain associated with the injection of BTX-A into the densely innervated skin of the palm or sole.[17] This is why many clinicians who contentedly treat axillary HH with BTX-A are reluctant to treat palmar and plantar HH; this procedure requires the use of a nerve block that entails even greater risks. Needle-free anesthesia may offer a new hope to overcome that stumbling block.[18] It may be used to extend the interinjection intervals of BTX-A, especially when its effect begins to wear off.

As the risk for antibody formation may increase with short interinjection intervals and high BTX-A single doses,[19] the use of aluminum chloride hexahydrate 10% to 55% in a gel vehicle, with or without SA 2% to 6% as an enhancer, becomes particularly relevant as a first line treatment, specifically in patients affected with focal HH at multiple sites. The formulation is most effective for sensitive intertriginous areas such as the axillae, groin, and anogenital and inframammary areas, but may also show a positive response in the face and scalp. It could also be of use in milder cases of palmoplantar HH, alone or in combination with other modalities. We should not expect a totally successful outcome at each and every treatment site, because even in instances where the result of the treatment is considered partial, the gel treatment may still have an overall positive impact on the patient

since fewer sites will be submitted to BTX-A injections. Consequently, by using a lower single dose of BTX-A, the patient's risk for antibody formation will be unlikely.

The treatment of focal HH, especially on the hands and feet, remains a therapeutic challenge. Knowledgeable pharmacists can be of great help by compounding aluminum chloride hexahydrate 15% in SA 2% gel to aluminum chloride hexahydrate 40% or higher with SA 4% to 6%. When successfully prepared, these extemporaneous formulations avert the need for more expensive treatments such as iontophoresis, BTX-A injections, or even surgery.[20]

SUMMARY

For focal HH, aluminum chloride hexahydrate 15% in SA 2% gel is a reasonable first line treatment, particularly in sensitive intertriginous areas. It could also be used as an adjunct treatment in cases of more resistant palmar and plantar HH, thus allowing the use of BTX-A where it is most needed.

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