A new strategy of iontophoresis for hyperhidrosis

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We used a modified iontophoretic method with an anticholinergic agent and aluminum chloride to treat hyperhidrosis. The strategy behind this combination was to shift gradually from inhibition of sweat gland secretion to blockage of the sweat duct. In a double-blind study in which we compared our method with tap water iontophoresis, the results were comparable. A second study revealed an 87% response rate, with an average remission period of 32 days. Our data indicate that patients who were older at onset, had a family history negative for the disorder, had an early response, or underwent treatment in cool weather had the most favorable results. (J AM ACAD DERMATOL 1990;22:239-41.)

Localized idiopathic hyperhidrosis is common and may cause social embarrassment and occupational problems. Topical application of aluminum chloride, formaldehyde, glutaraldehyde, or potassium permanganate produce only a short-term effect.[1-4] Systemic anticholinergic agents induce side effects before clinical improvement is noted. Surgery is often effective but has significant risks. Horner's syndrome, pleural effusion, phrenic nerve injury, or compensatory hyperhidrosis have been observed after surgical sympathectomy for palmar hyperhidrosis.[5]

Iontophoresis is defined as the electrical introduction of various ions through the skin. The most recently reported uses of iontophoresis are related to the control of localized idiopathic hyperhidrosis of the palms, soles, and axillae. Agents used in iontophoresis for hyperhidrosis include tap water and anticholinergic agents (e.g., atropine sulfate, glycopyrrolate or hexapyrrolate, and poldine methylsulfate).[6]

Hölzle and Alberti[7] observed that many patients undergo an initial increase in the intensity and frequency of sweating. This exacerbation usually subsides after three to five treatments. Significant improvement requires an average of 12 once-daily treatments for the hands and 10 once-daily treatments for the feet. On average, 1.3 treatments per week were necessary to maintain complete control of sweating.

Abell and Morgan[8] found that for treatment of hyperhidrosis iontophoresis with anticholinergic agents was more effective than with tap water, but marked side effects as a result of systemic absorption occurred. Hill et al.[9] reported that study of the sweat gland by light microscopy and transmission electron microscopy after tap water iontophoresis for palm hyperhidrosis revealed no structural change. In contrast, Hölzle et al.[10] reported that after long-term topical application of aluminum chloride, axillary eccrine glands showed necrosis of the lining epithelium; plugging, vacuolization, and atrophy of secretory epithelium; and accumulation of periodic acid–Schiff–positive, diastase-resistant material in the secretory coil lumen.

We combined iontophoresis of an anticholinergic agent and topical aluminum chloride to optimize therapeutic effects while minimizing side effects. We used an anticholinergic agent initially to inhibit sweat gland secretion and then applied aluminum chloride to produce structural changes in the sweat gland. Zankel and Durham[11] found that decreased sweating produced by local cooling increased the absorption of iodine 131. Thus the initial suppression of sweating by iontophoresis of an anticholinergic agent may increase the absorption of aluminum chloride and enhance its therapeutic effect.

MATERIAL AND METHODS

The patients were divided into two groups. The first, consisting of eight women and two men, was observed in a double-blind study in which one hand was treated with tap water iontophoresis alone and the other with our

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Table I. Protocol of combined iontophoresis

Day	Reaction time (min)	
	Glycopyrrolate 0.01%	Aluminum chloride 2%
1	30	0
2	20	10
3	10	20
4	0	30

Table II. Grading system of severity

3+	Dripping sweat
2+	Between 3+ and 1+
1	Slightly uncomfortable wetness
0	Comfortable at room temperature
1−	Uncomfortable dryness

combined method. The second group, consisting of 20 women and 10 men, was treated with the combined method on both hands (Table I).

Factors such as age, gender, age at onset, treated site, family history, occupation, season of treatment, and degree of seasonal severity were recorded. In the first group the severity of symptoms before and after treatment was recorded by iodine-starch paper (0, no print visible; 1+, faint dots, outline not discernible; 2+, faint print with clear outline; 3+, dark print with a ridged pattern and 4+, diffuse darkening, borders washed out). In the second group the severity of sweating was evaluated by patients subjectively (Table II).

The therapeutic agents included 0.01% glycopyrrolate (Robinul), 2% aluminum chloride, and tap water. The iontophoresis device involves the use of a rechargeable current source that supplies a direct current superimposed on a square-wave pulse with a frequency of 2 kHz and a 50% duty cycle. The stainless steel pans or rods were connected to the iontophoresis device by crocodile clips. The patients placed their hands in the pans or held the rods firmly in the axillae. The current was increased slowly until the patient felt some discomfort; the current was then allowed to flow for the specific period mentioned in the protocol. At the end of each treatment, the current was slowly reduced until it stopped. The polarity was then reversed, and the patient underwent the same procedure again. Iontophoresis with an anticholinergic agent was performed before iontophoresis with aluminum chloride. The treatment time was 1 hour daily.

RESULTS

The results of the first study are listed in Table III. Differences in the responses of the hands varied widely with tap water iontophoresis. The average

Table III. Comparison of therapeutic effects of tap water iontophoresis and combination iontophoresis

No. of patients ($n = 10$)	Decreased in severity in group after treatment*			Mean remission (days)†	
	Control	Study	Difference	Control	Study
2	−3	−3	0	5	28
2	0	−1	1	0	1
1	−1	−3	2	3	20
3	−2	−4	2	6	26
2	−1	−4	3	2	22
	(Mean −1.5)	(Mean −3.1)		(Mean 3.5)	(Mean 20)

*$p = 0.084 < 0.1$.
†$p = 0.098 < 0.1$.

decreases in severity after treatment were −1.5 with tap water iontophoresis and −3.1 with the combined method. The average remission period was 3.5 days with tap water iontophoresis and 20 days with the combined method. The differences of therapeutic efficacy between our method and tap water iontophoresis are obvious and statistically significant by the Kruskal-Wallis one-way ANOVA method.

In the second study no initial exacerbation of symptoms occurred during the first few treatments. In fact, 12 patients responded after 2 days of treatment and had an average remission period of 43 days after four once-daily treatments. Twenty-two patients responded after three treatments and had an remission period of 37 days after four treatments. On average, the response rate was 87% and the remission period was 32 days. Five patients noted peeling or vesiculation after 3 to 4 days of treatment. Only one patient noted transient mouth dryness. A seasonal variation of severity was noted. Twenty-five patients had more severe symptoms in summer and only one in winter. Four patients did not have any seasonal variation. Several patients with symptoms predominant in the summer noted longer remission periods in spring than in summer. Our results indicate that patients with a late age at onset, early response to treatment, and a family history negative for the disorder and patients who underwent treatment during cool weather had a more favorable outcome than other patients.

DISCUSSION

Akins et al.[12] reported that 8 of 10 hands, 3 of 9 feet, and 3 of 8 axillae responded clinically after 2 weeks of tap water iontophoresis. The time elapsed

until a significant decrease in sweating was noted (50% decrement) varied from 6 days (three hands) to more than 34 days (one foot). Three of 27 treated sites did not respond clinically within 1 month. These sites were treated for 30 minutes twice a day for the first 5 days and 30 minutes daily thereafter until the symptoms subsided. Akins et al.[12] also reported side effects in 27 treated sites, including 20 with a "pins and needles" sensation, 6 with vesicles, 6 with erythematous papules, and 9 with scaling.

Localized side effects are believed to be related to individual susceptibility, greater amperage,[7] longer treatment time, and dissociation of water into hydrogen or hydroxide ions.[13] The manufacturer of the Drionic compact iontophoretic device (General Medical Co., Los Angeles, Calif.) recently suggested a method of reducing the side effects of tap water iontophoresis. By presoaking the positively charged pad with a sodium bicarbonate solution, then rinsing the same pad every 10 minutes during treatment, the side effect caused by water dissociation could be prevented. Iontophoresis of salts with halogen (e.g., glycopyrrolate) produce fewer hydrogen ions at the positive pad. This phenomenon of water dissociation might explain why fewer side effects were reported in our study even when treatment time was doubled.

Abell and Morgan[8] reported that all of their 27 patients treated by iontophoresis with 0.1% glycopyrrolate noted marked dry mouth. The lower incidence of systemic side effects in our study probably was due to a lower drug concentration and a shorter treatment schedule.

In several previous studies the poorest therapeutic effect was on the axillae.[8, 14-17] With our method, results were as good in the axillae as in the hand and two patients noticed remissions of more than 5 months after only one course of treatment.

Our goals—an earlier response and better compliance—were achieved in this study. The 4-day treatment course was arbitrarily set by us for practicability of study and evaluation. Our combined therapy can be modified by the dermatologist according to the response time and the period of remission.

REFERENCES

1. Shelley WB, Laskas JJ, Satonove A. Effect of topical agents on plantar sweating. Arch Dermatol 1954; 69:713-6.
2. Juhlin L, Hansson H. Topical glutaraldehyde for plantar hyperhidrosis. Arch Dermatol 1968;97:327-30.
3. Gordon BI, Maibach HI. Eccrine anhidrosis due to glutaraldehyde, formaldehyde, and iontophoresis. J Invest Dermatol 1968;53:436-9.
4. Jensen O, Karlsmark T. Palmoplantar hyperhidrosis: treatment with alcoholic solution of aluminum chloride hexahydrate—a simple method of transpiration measurement. Dermatologica 1980;161:133-5.
5. Gruszkiewicz J, Doron Y, Guilburd JN, et al. Hyperhidrosis and its surgical treatment. Acta Neurochir 1986;81:128-31.
6. Sloan JB, Soltani K. Iontophoresis in dermatology: a review. J AM ACAD DERMATOL 1986;15:671-84.
7. Hölzle E, Alberti N. Long-term efficacy and side effects of tap water iontophoresis of palmoplantar hyperhidrosis: the usefulness of home therapy. Dermatologica 1987;175:126-35.
8. Abell E, Morgan K. The treatment of idiopathic hyperhidrosis by glycopyrronium bromide and tap water iontophoresis. Br J Dermatol 1974;91:87-91.
9. Hill AC, Baker GF, Jansen GT. Mechanism of action of iontophoresis in the treatment of palmar hyperhidrosis. Cutis 1981;28:69-72.
10. Hölzle E, Braun-Falco O. Structural changes in axillary eccrine glands following long-term treatment with aluminium chloride hexahydrate solution. Br J Dermatol 1984;110:339-403.
11. Zankel HT, Durham NC. Effect of physical modalities upon RaI iontophoresis. Arch Phys Med Rehabil 1963;44:93-7.
12. Akins DL, Meisenheimer JL, Dobson RL. Efficacy of the Drionic unit in the treatment of hyperhidrosis. J AM ACAD DERMATOL 1987;16:828-32.
13. Loewenthal LJA. Experimental miliaria. Arch Dermatol 1962;86:455-60.
14. Levit F. Treatment of hyperhidrosis by tap water iontophoresis. Cutis 1980;26:192-4.
15. Grice K, Sattar H, Baker H. Treatment of idiopathic hyperhidrosis with iontophoresis of tap water and poldine methosulphate. Br J Dermatol 1972;86:72-8.
16. Hölzle E, Ruzicka T. Treatment of hyperhidrosis by a battery-operated iontophoresis device. Dermatologica 1986; 172:41-7.
17. Stolman LP. Treatment of excess sweating of the palms by iontophoresis. Arch Dermatol 1987;123:893-6.