SHORT REPORT

Efficacy of iontophoresis with glycopyrronium bromide for treatment of primary palmar hyperhidrosis

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Abstract

Background There is limited data on the efficacy of iontophoretic treatment of primary palmar hyperhidrosis using glycopyrronium bromide. The first line treatment for primary palmar hyperhidrosis is usually topical aluminium chloride, but clinical experience indicates that it is not effective for more severe disease.

Objective To evaluate the efficacy of using glycopyrronium bromide iontophoresis in the treatment of primary palmar hyperhidrosis, and to evaluate if the benefit of treatment varies with the severity of disease.

Methods This is an open-label study involving patients undergoing weekly treatment of iontophoresis with glycopyrronium bromide for 4 weeks. Gravimetric measurements of sweat production and subjective scores of palmar sweatiness were recorded prior to starting treatment and 1 week after the last treatment. Side-effects were monitored weekly.

Results Twenty two of the 25 patients recruited completed the 4-week treatment. There was a significant mean improvement of 23.4 mg/min ($P = 0.001$) between baseline and post-treatment gravimetric measurements. Patients with a higher baseline sweat output demonstrated a trend towards a greater reduction in sweat production (Pearson's correlation correlation coefficient, $r = 0.41$). The patients experienced dryness of the palms for a mean duration of 5 days after iontophoresis. All patients reported an improvement in satisfaction scores and 81.8% reported an improvement in subjective severity scores. No serious side-effects were encountered during the study.

Conclusions Iontophoresis using glycopyrronium bromide is an effective and well-tolerated treatment for primary palmar hyperhidrosis. The possibility of its greater benefit in patients with more severe baseline disease requires verification.

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Conflict of interest

None.

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Introduction

Primary palmar hyperhidrosis is largely a clinical diagnosis.[1] The condition consists of varying severity and can significantly impact a persons' quality of life and interfere with their daily social and occupational activities.[2,3] The diagnosis of primary hyperhidrosis requires the exclusion of generalized hyperhidrosis due to systemic disorders and focal hyperhidrosis because of a neurological pathology. Treatment options typically consist of topical aluminium chloride, iontophoresis, botulinum toxin injection, systemic anticholinergic drugs and endoscopic thoracic sympathectomy. Topical aluminium chloride is usually the first line therapy for palmar hyperhidrosis,[4] but clinical experience suggests that it is not usually effective for more severe disease.

Iontophoresis has been used for many years and various agents have been used, namely tap water, anticholinergic agents (such as glycopyrronium bromide, poldine methylsulphate, atropine sulphate and methanthelinium bromide) and aluminium chloride. Anticholinergic drugs have been shown to be more effective than tap water,[5–8] but their efficacy has not been well evaluated. Systemically absorption of these anticholinergic agents can cause side-effects such as dry mouth and eyes, constipation and urinary retention; however, the incidence of side-effects varies widely across different studies.

Objective

The aims of this study were to evaluate the efficacy of iontophoresis using glycopyrronium bromide in the treatment of primary palmar hyperhidrosis and to determine if the benefit of treatment varies with the severity of disease.

Methods

Patient selection

This was an open-label study with patients recruited from the general dermatology clinics in the National Skin Centre (Singapore) from April 2009 to March 2010. Patients diagnosed with primary palmar hyperhidrosis, with no topical, oral anticholinergics or iontophoretic treatment in the previous 1 month and without previous botulinum toxin injection or sympathectomy, were recruited. Patients who were pregnant or lactating, with a history of ischaemic heart disease, arrhythmias or narrow angle glaucoma, with metal implants like a pacemaker, and patients who were older than 60 years old or younger than 13 years old were excluded. This study was approved by the country's research ethics committee, and all patients gave written informed consent.

Iontophoresis protocol

Patients underwent weekly treatments of iontophoresis with glycopyrronium bromide for 4 weeks. Iontophoresis was performed with a single machine (Ionos 7 freeline, Nemectron, Germany). The setup consisted of two trays, each containing a flexible electrode in a double varicose cover, with a plastic lattice placed above each electrode. The tray that contained the anode was filled with glycopyrronium bromide 0.04% solution and the tray containing the cathode was filled with tap water. The alternating electrical current was increased slowly till a maximum comfortable current was achieved. The current was allowed to pass for 10 min, after which the trays (together with the electrodes) were switched to the other hand. The current was again allowed to pass for 10 min.

Assessment of severity and response

The objective and subjective severity of hyperhidrosis was assessed at baseline and 1 week after the fourth iontophoresis treatment.

The objective assessment consisted of gravimetric measurement of sweat production and this was performed in a private, quiet room with the room temperature set at 25 °C. Each patient was asked to place his/her palms on a large piece of filter paper that was preweighed using a micro-scale (*Libor EB*-330H, *Shimadzu*, Japan). After 5 min, the filter paper, having absorbed the sweat produced, was weighed again. The difference in weight was used to calculate the sweat produced per minute.

The subjective assessment was performed by asking the patients to grade their usual level of sweatiness as moist, wet or dripping with sweat. They were also asked to score their satisfaction level of their condition on a scale of 1–5 (1 indicates very dissatisfied, 3 indicates neither satisfied nor dissatisfied and 5 indicates very satisfied).

After each weekly iontophoresis, the number of days each patient experienced dryness of his/her palms were recorded.

Assessment of adverse events

After each iontophoresis treatment and before the next, the patients were assessed for any local or systemic adverse effects.

Statistical analysis

Statistical analysis was performed using the paired Wilcoxon signed-rank test (with a P-value of <0.05 considered significant) and the Pearson product-moment correlation coefficient.

Results

Subjects

Twenty-five patients were sequentially recruited and 22 patients completed the 4 weeks of treatment. Two patients withdrew because of time constraints, and one patient withdrew after experiencing mild vesiculation of the hands after the first iontophoresis treatment.

The mean age of the patients was 23.9 years (range 13–51 years); 63.6% of the patients were men and the majority of them were Chinese (95.5%). The mean baseline gravimetric measurement was 45.8 mg/min (range 12–94.4 mg/min), and 9.1%, 77.3% and 13.6% of patients described their palms as moist, wet and dripping with sweat respectively. At baseline, 72.7% of patients were dissatisfied with the control of their condition (with a score of 1 or 2).

Iontophoretic protocol

The mean current used during iontophoresis was 4.7 mA (range 2.5 mA–7.1 mA). There was no correlation between the degree of improvement measured via gravimetric assessment and the mean current tolerated by the subject (Pearson's correlation coefficient, $r = -0.29$)

Difference in objective measurements

The mean gravimetric measurements were 45.85 mg/min before treatment (range 12–94.4 mg/min) and 22.45 mg/min after treatment (range 1.6–63.8 mg/min). This improvement of 23.4 mg/min is statistically significant ($P = 0.001$) (Table 1). Patients with a higher baseline sweat output demonstrated a trend towards a greater reduction in sweat production (Pearson's correlation coefficient, $r = 0.41$).

Difference in subjective measurements

All patients reported an improvement in satisfaction scores with a significant increase in post-treatment satisfaction scores ($P < 0.0005$). The mean satisfaction score before treatment was 1.9 and that after treatment was 3.9. With regards to the subjective

Table 1 Comparison of pre- and post-treatment gravimetric measurement

Patient number	Pretreatment gravimetric measurement (mg/min)	Post-treatment gravimetric measurement (mg/min)	% Difference
1	12	31.8	−165
2	15.8	5	68.35
3	20.4	15	26.47
4	22	13	40.91
5	25.2	16	36.51
6	26	5.8	77.69
7	35	29.6	15.43
8	40.6	1.8	95.57
9	40.8	32.6	20.1
10	41	29.8	27.32
11	42	22.6	46.19
12	48.4	41	15.29
13	51.4	63.8	−24.12
14	51.4	1.6	96.89
15	52	54.6	−5
16	58.4	25	57.19
17	65.8	2.4	96.35
18	72.2	30.8	57.34
19	88.6	22.6	74.49
20	94.4	28.4	69.92
21	58	12.2	78.97
22	47.2	8.6	81.78

There was a significant mean decrease of sweat production of 23.4 mg/min ($P = 0.001$) between baseline (45.85 mg/min) and after four iontophoresis treatments (22.45 mg/min).

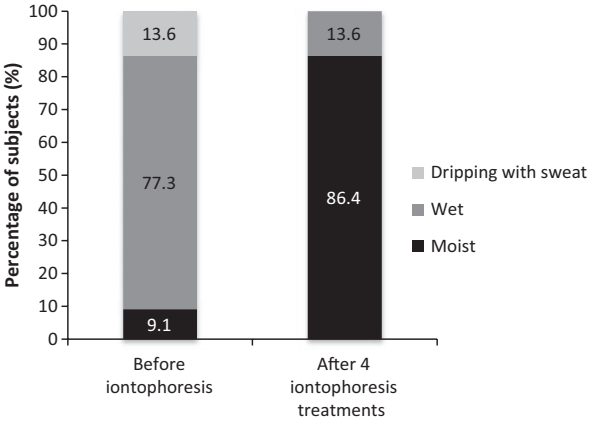

Figure 1 81.8% of the subjects reported an improvement in subjective severity scores after four iontophoresis treatments. Prior to treatment, 9.1%, 77.3% and 13.6% of subjects described their palms as moist, wet and dripping with sweat respectively. After treatment, 86.4% and 13.6% of subjects describing their palms as moist and wet respectively.

severity score, 81.8% of patients reported improvement after treatment (Fig. 1). After four iontophoresis treatments, the mean reported duration of palm dryness was 5 days.

Side-effects

No serious side-effects were encountered during the study. The majority of the patients (91%) experienced systemic side-effects, with dry mouth or throat being the commonest and occurring in all patients. All patients reported mild local adverse effects with dysaesthesia during treatment being commonest, followed by irritation of the hands along the water line (86.4%), getting a small shock when moving hands out of the water tray (68.2%), dermatitis (45.5%), asteatosis after repeated treatments (27.3%) and vesiculation of the hands (18.2%).

Discussion

Iontophoresis using glycopyrronium bromide has been used for the treatment of palmar hyperhidrosis for many years, but no study has objectively evaluated its efficacy. This study aims to evaluate the efficacy of glycopyrronium bromide iontophoresis both objectively and subjectively.

There was a significant mean decrease in palmar sweat production of 23.4 mg/min after four iontophoresis treatments and this correlated with the improvement in subjective severity and satisfaction scores. Although limited by the small number of patients in this study, there is a trend that patients with a greater baseline sweat production have a greater percentage improvement after treatment. The clinical implication of this result is that in patients with more severe disease, iontophoresis with glycopyrronium bromide may be considered as the treatment modality early in the course of managing the disease.

Previous studies have reported widely varying incidence of systemic side-effects with the use of anticholinergics in iontophoresis. In our study, the systemic side-effects were generally mild and well-tolerated. All patients had experienced local side-effects, but only one patient had to stop treatment. Iontophoresis using glycopyrronium bromide appears to be safe and well-tolerated in our series of patients. Based on the anticholinergic systemic side-effects experienced by our patients, it is plausible that the mechanism of action of iontophoresis with glycopyrronium bromide is via systemic absorption of the anticholinergic.

The production of sweat is under the control of the sympathetic nervous system from the brain. In this study, we wanted to evaluate the overall efficacy of iontophoretic treatment, including its placebo effect. The use of tap water as a control would not be appropriate, as previous studies had shown that iontophoresis using tap water alone is effective in treating hyperhidrosis.[9,10] A left-right hand comparison would also not be appropriate, as systemic absorption of the anticholinergic drug from one hand would result in dryness of the other hand.

Conclusions

Iontophoresis using glycopyrronium bromide is an effective and well-tolerated treatment for primary palmar hyperhidrosis. The possibility of its greater benefit in patients with more severe baseline disease requires verification.

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