Acta Derm Venereol 2010; 90: 291–293

CLINICAL REPORT

Treatment of Generalized Hyperhidrosis with Oxybutynin in Postmenopausal Patients

Won Oak KIM, Hae Keum KIL, Kyung Bong YOON and Ji Hyun YOO
Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, South Korea

Postmenopausal hyperhidrosis is a form of secondary hyperhidrosis, and hormone-replacement therapy is a commonly used therapeutic option. However, some women do not benefit from this treatment, and oral anticholinergics are a logical alternative for reducing generalized sweating in these patients. Twenty-one patients were medicated with 5 or 10 mg of oxybutynin per day. After a 3-month follow-up period, efficacy was assessed with the Hyperhidrosis Disease Severity Scale (HDSS) and the Dermatology Life Quality Index (DLQI) was used to assess the improvement in patients' quality of life. The HDSS score was 3.2 ± 0.4 (mean ± SD) before medication and 1.9 ± 0.4 after 3 months. The baseline DLQI score of 8.4 ± 1.0 was reduced to 4.4 ± 0.9. No serious side-effects or adverse events resulted from treatment. Oxybutynin was a well-tolerated, effective, and safe method for treating postmenopausal sweating. However, long-term medication and the limited effects of the treatment were disadvantages. ***Key words: oxubutynin; hyperhidrosis; postmenopause.***

(Accepted November 3, 2009.)

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Won Oak Kim, Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, 134 Sinchon-dong, Seodaemun-gu, Seoul 120-75, Korea. E-mail: wokim@yumc.yonsei.ac.kr; drwokim@hanmail.net

Hyperhidrosis is a benign sympathetic disorder that results in excessive sweating beyond the level needed to cool elevated body temperature. It may have a negative effect on the patient's quality of life. Excessive sweating disorders can be classified as primary or secondary hyperhidrosis according to their aetiology. Primary hyperhidrosis is idiopathic and focal, with a genetic predisposition, and sweating is often induced as a response to emotional stimuli. Secondary hyperhidrosis may be generalized, and is frequently associated with diseases or side-effects of several drugs that alter the set point of temperature in the hypothalamus (1, 2). Postmenopausal hyperhidrosis is classified as secondary hyperhidrosis, and generalized sweating is not a rare manifestation of vasomotor symptoms. According to the Menopause Epidemiology Study in the USA, the prevalence of vasomotor symptoms is 79% in perimenopausal and 65% in postmenopausal women. Frequency (severity) of night sweats every night was an average of 2.4 (moderate), 3.2 (severe), and 2.7 (very severe night sweats) in a typical night (3).

Various treatments, including hormone-replacement therapy, have been used with the aim of alleviating symptomatic hyperhidrosis. The non-hormonal therapies used include gabapentin, selective serotonin reuptake inhibitors, serotonin noradrenaline reuptake inhibitors, acupuncture, and herbal medication.

Anecdotal evidence and a study of a series of patients have demonstrated that generalized hyperhidrosis can be treated successfully with oral oxybutynin (2, 4–6). Here, we evaluated the safety and effectiveness of oxybutynin through our prospective analysis of postmenopausal patients who were treated successfully with oxybutynin for generalized hyperhidrosis.

PATIENTS AND METHODS

We reviewed 21 consecutive patients (mean age ± standard deviation (SD): 54.1 ± 4.5 years) from November 2004 to December 2008 who were treated at the Hyperhidrosis Clinic of the Yonsei University Health System for moderate to severe generalized hyperhidrosis after menopause. These patients had been experiencing sweating that was not improved by conservative treatments such as hormone-replacement therapy or other non-hormonal therapeutic options. We focused only on patients' sweating symptoms in order to select women who were suitable for treatment. The inclusion criteria were secondary and postmenopausal hyperhidrosis with generalized sweating. The exclusion criteria were history of possible concurrent underlying disease and use of sweat-inducing drugs within the previous month. All patients were given complete information about the oxybutynin treatment and its possible complications. Written informed consent was obtained from each patient. The study was audited through the departmental research briefing, and all protocols were in accordance with the ethical principles defined by the Declaration of Helsinki.

A subjective diagnosis was made following careful history-taking and a physical examination. Objective evaluations of sweating, such as the Minor's iodine-starch test, gravimetric test, hygrometric test, or colorimetric test, were not performed because whole-body sweating or night sweating were clear subjective experiences. Blood pressure, routine blood chemistry, and hormonal studies were conducted in some patients in order to rule out other causes of hyperhidrosis. To evaluate the effective dosage, each patient was instructed to take 5 mg of oxybutynin every day in the morning for one week. If 5 mg of oxybutynin was insufficient to reduce sweating, an additional 5 mg was administered in the evenings. Patients were asked to telephone or e-mail us if they noticed side-effects.

On return visits after the first week, patients were prescribed oxybutynin for 3 months unless they refused to continue the treatment. Patients' subjective observations and experiences were evaluated with a questionnaire 3 months later. Efficacy was measured by the patients' assessment of the tolerability of sweating and interference effect of sweating on daily activities on the 4-point Hyperhidrosis Disease Severity Scale (HDSS) (Table I) (7). The HDSS scores were analysed by comparing scores at baseline with scores reported 3 months after treatment. The Dermatology Life Quality Index (DLQI) is a self-reported questionnaire designed to measure the impact of skin diseases on patients' quality of life (8). Baseline and follow-up assessments of the total DLQI scores were calculated to evaluate the change in the score.

Statistical analyses were performed using SPSS 13.0 for Windows. The two-sided Wilcoxon signed-rank test for paired samples was used to compare the efficacy of oxybutynin. A p-value less than 0.05 was considered statistically significant for each analysis.

RESULTS

Patients first recognized excessive sweating at a mean age of 50.6 ± 3.9 years, and had the symptom for a mean duration of 3.5 ± 1.8 years. No patients had a previous history of primary hyperhidrosis. Sweating was not confined to night episodes in any patient. Twelve patients had a history of hormone-replacement therapy, varying from 6 to 18 months, and three patients were still undergoing hormone-replacement therapy. Five patients had tried non-hormonal therapy.

The dose of oxybutynin was 5 mg (19 patients) or 10 mg (2 patients) according to the patient's need. The baseline HDSS score was 3.2 ± 0.4. All patients showed at least a 1.0-point improvement in HDSS score from baseline to 3 months (1.9 ± 0.4) after oxybutynin treatment ($p < 0.01$) (Table II). Sweating was reduced within 2 days after oxybutynin treatment. However, two patients still experienced an uncomfortable level of sweating from time to time, albeit at a reduced rate. The baseline DLQI score was 8.4 ± 1.0, which decreased to 4.4 ± 0.9 ($p < 0.01$) 3 months after treatment (Table II).

No patients reported serious side-effects or adverse events during oxybutynin treatment or at follow-up. Minor side-effects, such as dry mouth, occurred in three patients, and slight urinary difficulties (feeling of mild urinary retension) occurred in one patient. However, these symptoms were mild and were tolerated without any additional treatment. Five of 7 patients with mild to moderate symptoms of urinary incontinence reported that their urinary incontinence was relieved after treatment. None of the patients showed side-effects such as dry eyes, dizziness, diarrhoea, mydriasis, flushing, and rashes.

Seventeen patients had hot flushes and two patients experienced palpitations that were not reduced or eliminated after oxybutynin administration. We did not observe any other postmenopausal symptoms, including sleep disturbance, nervousness, depression, vertigo, headache, fatigue, arthralgia, and vaginal dryness during the study.

Table I. *Hyperhidrosis Disease Severity Scale (HDSS)*

How would you rate the severity of your sweating?	Score
My generalized sweating is never noticeable and never interferes with my daily activities.	1
My generalized sweating is tolerable but sometimes interferes with my daily activities.	2
My generalized sweating is barely tolerable and frequently interferes with my daily activities.	3
My generalized sweating is intolerable and always interferes with my daily activities.	4

Table II. *Individual and mean ± SD scores (all female) on the Hyperhidrosis Disease Severity Scale (HDSS) and Dermatology Life Quality Index (DLQI) before and after 3 months of oxybutynin therapy*

		HDSS score		DLQI	
Pat. No.	Age	Before	After	Before	After
1	58	4	2	9	5
2	57	3	2	8	4
3	61	3	2	8	5
4	60	3	2	10	4
5	62	4	2	8	3
6	57	3	1	9	4
7	51	3	2	9	4
8[a]	51	3	2	7	5
9	48	3	2	8	4
10	55	4	2	8	6
11	49	3	2	8	3
12	51	3	2	10	5
13	53	3	1	8	4
14	53	3	2	10	6
15	52	3	2	7	5
16	57	4	2	9	4
17	50	3	2	8	5
18	60	3	1	7	3
19	53	4	2	8	4
20	46	3	2	10	4
21[a]	52	3	2	7	6
Mean ± SD	54.1 ± 4.5	3.2 ± 0.4	1.9 ± 0.4[a]	8.4 ± 1.0	4.4 ± 0.9[b]

[a]The patient received the higher dose of 10 mg drug.
[b]$p < 0.01$

DISCUSSION

Secondary hyperhidrosis manifesting as generalized sweating may be associated with various systemic causes, including menopause, and the mechanism of the change in sensitivity of the hypothalamic set point remains unclear. However, symptoms that are alleviated by hormone-replacement therapy suggest that the cause is falling levels of oestrogen. Oestrogen ameliorates hot flushes by increasing the sweating threshold in the thermo-neural zone (9). As a result, hormone-replacement therapy, which was introduced approximately 70 years ago, was once considered the gold standard for the treatment of menopausal symptoms. Nowadays the use of hormone-replacement therapy is prescribed only after taking into account its risks and benefits (10). Consequently, a large number of women choose not to receive hormone-replacement therapy, and seek alternatives, such as phyto-oestrogens and selective

oestrogen receptor modulators, in an attempt to relieve vasomotor symptoms and sweating. Anticholinergics are expected to be more powerful for controlling sweating than conventional therapies.

Although oral anticholinergics have been used for more than two decades, side-effects may limit their use in treatment. Propantheline, glycopyrrolate, oxybutynin, and benzotropine may be effective (11, 12). Glycopyrrolate and oxybutynin are thought to pose fewer unwanted effects than other anti-cholinergics, such as atropine, and both have been used in treatment of hyperhidrosis (2, 5, 6). They reduce the action of acetylcholine on sweat glands, and have a lesser affinity for crossing the blood-brain barrier unlike other anticholinergics. Therefore, they are less likely to produce side-effects (5). Oxybutynin is frequently administered to prevent pollakisuria and hyper-reflectory urine bladder because of its antispasmodic and anticholinergic effects at a maximal dose of 20 mg daily. In our study (13) we assessed the effectiveness of low doses of oxybutynin during a 3-month follow-up period in hyperhidrosis patients.

An objective assessment, such as gravimetric measurement, does not take the patient's daily activity and quality of life into account (14). The patient's distress due to sweating is subjective to personal experience that the degree and patterns of sweating may vary considerably from moment to moment dependent on factors such as the time of day and emotional stimuli (15). In comparison with gravimetric measurements, which merely assess the quantitative sum of sweating, HDSS measures the effectiveness of therapy via patients' subjective assessment of their tolerability of sweating. In addition, we also used the DLQI as a subjective evaluation of the disability caused by sweating. The self-evaluation scale was confirmed as useful in assessing research or clinical protocols to provide the necessary validation in wider spectra of patients (16).

In our study, the mean HDSS and DLQI scores before oxybutynin treatment were high, indicating that patients with moderate to severe postmenopausal hyperhidrosis are considerably impaired in their daily activities, and that the adverse effects of excessive sweating decreases their quality of life. Our assessment of the changes in HDSS and DLQI in response to oxybutynin treatment showed that oxybutynin treatment resulted in the reduction of HDSS and DLQI scores. However, this result was less favourable than in another open-label study that was conducted on patients who had diverse causes of idiopathic sweating with generalized hyperhidrosis (6). In Tupker's study, baseline DLQI scores were higher (15.9 ± 6.9) than those of our patients' (8.4 ± 1.0). Old age and culturally-defined acceptance of sweating in our patients seem to be a reason. The study of Tupker et al. also showed a greater decrease in the score to 3.7 ± 5.2 after treatment and a higher incidence of adverse effects with fixed doses (2.5 mg 3 times daily/5 mg 3 times daily). Although our final score of 4.4 ± 0.9 was higher, the incidence of side-effects was lower due to a low dose of oxybutynin (5 mg, once daily) or a long-term interval of a dosing regimen (5 mg in the morning and evening).

Our study supports previous findings that oral administration of oxybutynin effectively reduces generalized sweating in secondary hyperhidrosis (6). Moreover, no patients demonstrated drug intolerance to oral intake of oxybutynin during the 3-month follow-up period. The need for sustained administration is the main drawback. Although our present evaluation has limitations inherent to an open-label study, oxybutynin therapy seems to provide a simple, safe and reasonably effective treatment for severe postmenopausal sweating.

The authors declare no conflicts of interest.

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