A randomized placebo-controlled trial of oxybutynin for the initial treatment of palmar and axillary hyperhidrosis

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Introduction: Video-assisted thoracic sympathectomy provides excellent resolution of palmar and axillary hyperhidrosis but is associated with compensatory hyperhidrosis. Low doses of oxybutynin, an anticholinergic medication that competitively antagonizes the muscarinic acetylcholine receptor, can be used to treat palmar hyperhidrosis with fewer side effects.

Objective: This study evaluated the effectiveness and patient satisfaction of oral oxybutynin at low doses (5 mg twice daily) compared with placebo for treating palmar hyperhidrosis.

Methods: This was a prospective, randomized, and controlled study. From December 2010 to February 2011, 50 consecutive patients with palmar hyperhidrosis were treated with oxybutynin or placebo. Data were collected from 50 patients, but 5 (10.0%) were lost to follow-up. During the first week, patients received 2.5 mg of oxybutynin once daily in the evening. From days 8 to 21, they received 2.5 mg twice daily, and from day 22 to the end of week 6, they received 5 mg twice daily. All patients underwent two evaluations, before and after (6 weeks) the oxybutynin treatment, using a clinical questionnaire and a clinical protocol for quality of life.

Results: Palmar and axillary hyperhidrosis improved in >70% of the patients, and 47.8% of those presented great improvement. Plantar hyperhidrosis improved in >90% of the patients. Most patients (65.2%) showed improvements in their quality of life. The side effects were minor, with dry mouth being the most frequent (47.8%).

Conclusions: Treatment of palmar and axillary hyperhidrosis with oxybutynin is a good initial alternative for treatment given that it presents good results and improves quality of life. (J Vasc Surg 2012;55:1696-700.)

Sweating is a physiologic mechanism of human thermoregulation. Hyperhidrosis, a disease that affects 2.8% of the population, is a somatic disorder characterized by exaggerated sweating in a specific region due to hyperfunctioning of the sweat glands. It is frequently triggered by emotions and leads to serious emotional disturbances in many patients.

Palmar hyperhidrosis (PH) and axillary hyperhidrosis (AH) are the most frequent clinical manifestations of primary hyperhidrosis, and video-assisted thoracic sympathectomy (VATS) is the most appropriate definitive treatment, with high success rates and low risk. However, some complications are observed with surgical denervation, the most frequent being compensatory hyperhidrosis, with an incidence >75% and with an unknown pathophysiology. In about 30% of patients, compensatory hyperhidrosis is intense enough to generate dissatisfaction with VATS.

Different anticholinergic drugs have been used to treat hyperhidrosis, but their use has not become routine because of side effects. Oxybutynin is an anticholinergic drug that has been used safely at high doses (up to 15 mg/d) to treat micturition disorders, and a side effect observed in these patients has been diminished sudoresis. The use of oxybutynin for treating primary hyperhidrosis has only been described in three case reports, one series of 14 patients with compensatory hyperhidrosis after VATS, one publication about facial hyperhidrosis, and one publication of PH. To our knowledge, no studies have compared the use of oxybutynin vs placebo in the treatment of PH or AH.

Considering that the main treatment for PH and AH is surgery and that the side effects of such treatment are significant, oxybutynin represents a possible alternative. This study investigated patient satisfaction and the effectiveness of low doses of oxybutynin for treating PH or AH in a randomized, prospective, blind, and controlled trial.

METHODS

This was a prospective, randomized, controlled, study in which the patients were blinded. The institutional protocol applied to the patients was in accordance with the principles of the Ethics Committee for Analysis of Research Projects on Human Experimentation.

The criterion for inclusion in the study was a complaint of PH or AH with the intention of using a new medication after information about the risks and side effects. The
participants were specifically told that dry mouth was the most frequent side effect and the others were minor and fleeting. The exclusion criteria were previous glaucoma, urinary retention, gastric retention, narrow-angle glaucoma, and demonstrated hypersensitivity to the drug substance or other components of the product.

This was a prospective, randomized, and controlled study. From January to June 2011, 50 consecutive patients with PH or AH were included. Of these, 25 patients were assigned for treatment with oxybutynin and 25 for placebo. Three patients from the placebo group (PG) and two from the oxybutynin group (OG) were lost to follow-up. All patients were evaluated on two occasions: before the medication was prescribed and after 6 weeks of treatment.

The PG patients were sex-matched and age-matched with the OG patients. The distribution of age, sex, and hyperhidrosis site is summarized in Table I. In addition to PH and AH, 12 OG patients and 15 PG patients presented with plantar hyperhidrosis as well.

Oxybutynin was prescribed for 6 weeks in progressively increasing doses throughout treatment. At their first visit, the patients were given 2.5 mg to be taken once daily in the evening. They were instructed to increase the dose to 2.5 mg twice daily from days 8 to 21. After this period, patients had a second visit, and the oxybutynin dose was increased to 5 mg twice daily from day 22 to the end of the day 42, when a third visit was scheduled. The PG received the same instructions.

After inclusion, the patients were asked to complete a validated questionnaire about the negative effect of hyperhidrosis on their quality of life (QOL) using a protocol that was adapted to English. After 6 weeks of treatment, patients were asked to complete two additional questionnaires: one about improvement in the symptoms, including side effects, and other about improvement in QOL. They evaluated improvement in hyperhidrosis on a scale from 0 (no improvement) to 10 (absence of hyperhidrosis), based on their own estimates without any intervention or advice from the interviewer. For data analysis, the improvement was recorded as null or slight when it was 0 to 4, moderate when it was 5 to 7, or great when it was 8 to 10.

The negative effect of hyperhidrosis on QOL before the treatment was classified into five levels and calculated as the summed total score from the protocol (range, 20-100). Higher levels indicated greater severity and poorer QOL. When the total was >84, the QOL was considered as very poor; from 68 to 83, poor; from 52 to 67, good; from 36 to 51, very good; and from 20 to 35, excellent.

Improvement of QOL after the treatment was also classified using five levels. When the total was >84, the QOL was considered as much worse; from 68 to 83, a little worse; from 52 to 67, the same; from 36 to 51, a little better; and from 20 to 35, much better.

Patients evaluated the presence of dry mouth on a scale from 0 to 3, where 0 represented absence; 1, mild; 2, moderate; and 3, severe.

The following parameters were studied: evolution of PH and AH, evolution of hyperhidrosis at the feet, negative effect of hyperhidrosis on QOL before the treatment, improvement in QOL after the treatment, complications, and side effects.

Statistical analysis. The $\chi^2$ test was performed to verify the association between categoric variables in contingency tables, and the Student $t$-test was used to compare age and study group. The significance level considered for all statistical tests was 0.05.

RESULTS

The evolution of PH and AH for both groups is presented in Table II. A significant association was observed between the evolution and study groups, with >70% of OG patients experiencing moderate or great improvement in PH or AH, whereas only 27.3% of PG patients had moderate improvement ($P < .001$). The evolution of plantar hyperhidrosis for both groups is presented in Table III. A significant association was observed between the evolution and study groups, with more than 90% of the OG patients experiencing moderate or great improvement in plantar hyperhidrosis, whereas only 15.4% of PG patients had moderate improvement ($P < .001$).

The effect of hyperhidrosis on QOL before the treatment is presented in Table IV. Before the treatment, all patients fell into the poor or very poor categories; a nonsignificant difference was observed between groups and

### Table I. Age, sex, and hyperhidrosis site distribution in each study group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo ($n = 22$)</th>
<th>Oxybutynin ($n = 23$)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>Median (range)</td>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>28.0 (18-48)</td>
<td>25.5 (18-50)</td>
<td>. . .</td>
</tr>
<tr>
<td>Sex, No.</td>
<td>Male 6</td>
<td>Female 16</td>
<td>. . .</td>
</tr>
<tr>
<td>Hyperhidrosis site, No.</td>
<td>Palmar 10</td>
<td>11</td>
<td>. . .</td>
</tr>
<tr>
<td></td>
<td>Axillary 12</td>
<td>12</td>
<td>. . .</td>
</tr>
</tbody>
</table>

SD, Standard deviation.

$^a$P value was obtained by Student t-test.

$^b$P value was obtained by $\chi^2$ test.

### Table II. Evolution of palmar or axillary hyperhidrosis, or both

<table>
<thead>
<tr>
<th>Evolution</th>
<th>Placebo No. (%)</th>
<th>Oxybutynin No. (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worse</td>
<td>(0.0)</td>
<td>0 (0.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Null/slight</td>
<td>16 (72.7)</td>
<td>6 (26.1)</td>
<td>. . .</td>
</tr>
<tr>
<td>Moderate</td>
<td>6 (27.3)</td>
<td>6 (26.1)</td>
<td>. . .</td>
</tr>
<tr>
<td>Great</td>
<td>0 (0.0)</td>
<td>11 (47.8)</td>
<td>. . .</td>
</tr>
<tr>
<td>Total</td>
<td>22 (100)</td>
<td>23 (100)</td>
<td>. . .</td>
</tr>
</tbody>
</table>

$^a$P value was obtained by $\chi^2$ test, excluding worse (0 cases).
Table III. Evolution of plantar hyperhidrosis

<table>
<thead>
<tr>
<th>Evolution</th>
<th>Placebo No. (%)</th>
<th>Oxybutynin No. (%)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worse</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Null/slight</td>
<td>13 (86.6)</td>
<td>1 (8.3)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (13.4)</td>
<td>7 (58.3)</td>
<td></td>
</tr>
<tr>
<td>Great</td>
<td>0 (0.0)</td>
<td>4 (33.4)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>15 (100)</td>
<td>12 15 (100)</td>
<td></td>
</tr>
</tbody>
</table>

aP value was obtained by χ² test, considering worse + null/slight vs moderate + great.

Table IV. Impact of hyperhidrosis on quality of life (QOL) before the treatment

<table>
<thead>
<tr>
<th>QOL before treatment</th>
<th>Placebo No. (%)</th>
<th>Oxybutynin No. (%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>84-100 (very poor)</td>
<td>16 (72.7)</td>
<td>15 (65.2)</td>
<td>.426</td>
</tr>
<tr>
<td>68-83 (poor)</td>
<td>6 (27.3)</td>
<td>8 (34.8)</td>
<td></td>
</tr>
<tr>
<td>52-67 (good)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>36-51 (very good)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>20-35 (excellent)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>22 (100)</td>
<td>23 (100)</td>
<td></td>
</tr>
</tbody>
</table>

aP value was obtained by χ² test, considering very poor vs poor.

Table V. Improvement in quality of life (QOL) after treatment

<table>
<thead>
<tr>
<th>Level of improvement</th>
<th>Placebo No. (%)</th>
<th>Oxybutynin No. (%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-35 (much better)</td>
<td>0</td>
<td>8 (34.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>36-51 (a little better)</td>
<td>3 (13.6)</td>
<td>9 (39.1)</td>
<td></td>
</tr>
<tr>
<td>52-67 (the same)</td>
<td>19 (86.4)</td>
<td>6 (26.1)</td>
<td></td>
</tr>
<tr>
<td>68-83 (a little worse)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>84-100 (much worse)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>22 (100)</td>
<td>23 (100)</td>
<td></td>
</tr>
</tbody>
</table>

aP value was obtained by χ² test.

levels of QOL (P = .426). The median QOL was 87.5 ± 9 for PG and 91 ± 8 for OG. The improvement in QOL after the treatment is presented in Table V. The difference between the OG and PG (73.9% vs 13.6%) was significant (P < .001).

The only side effect observed in this series was the presence of dry mouth, which is presented in Table VI. Almost 30% of the patients in the two groups had moderate or severe dry mouth after 3 weeks. After 6 weeks (with higher doses), the frequency decreased for 9.1% in PG but increased for 34.8% in OG.

DISCUSSION

The excellent results of VATS in treating patients with PH and AH have led to an increasing demand for treatment worldwide. Most patients have been women in their early 20s because excessive sweating has greater repercussions in women’s day-to-day lives and so they are more likely to seek treatment. The symptoms usually start during childhood, and they look for treatment when they are young adults.

Patients whose urinary disorders are treated using oxybutynin take larger doses (15 mg/d) than those used to treat hyperhidrosis (10 mg/d) and may experience side effects of greater severity (dry mouth, headache, and urine retention). We decided to start the treatment with very low doses of oxybutynin (2.5 mg/d) and to progressively increase the dose up to 10 mg/d, because patients with urinary disorders who start treatment with 10 mg/d usually feel severe mouth dryness at the onset of treatment.

In this study, the application of the placebo, a pharmacologically inert substance that produces similar effects to what would be expected, made it possible to distinguish the pharmacologic results and side effects from those that were not caused by the drug. We found that the incidence of dry mouth was similar to the placebo effect only in the beginning of the treatment. In this phase (until day 21), with a minimum dose of oxybutynin, the incidence of severe or moderate dry mouth was ~30% in both groups. This effect demonstrates the power of verbal instructions about this collateral effect and probably demonstrates that every individual feels thirst during the day at certain moments and unconsciously ingests liquids to quench their thirst, and it also demonstrates that patients may pay more attention to the regular sensation of thirst because of these instructions. If we had told them that another specific effect was likely, it probably would have been reported by the patients.

With the increase of the dosage, 34.8% of the patients using 10 mg of oxybutynin had the sensation of moderate or severe dry mouth, whereas the placebo’s effect of dry mouth decreased to 9.1% (final placebo effect). Oxybutynin was well tolerated despite this symptom (dry mouth), and none of the patients abandoned the treatment due to this symptom. Additional data to this study are that after the protocol period, >50% of the patients (those who had improved and did not want to undergo an operation) continued using the medication, and dry mouth was not an impeding factor.

These patients with hyperhidrosis described great discontent with their PH or AH in our specific QOL questionnaire on hyperhidrosis, which has been validated and used in several published studies. The degree to which hyperhidrosis lowers a patient’s QOL depends on the severity of the condition and the patient’s adaptation to each situation. Some individuals with milder hyperhidrosis report a very poor QOL, whereas others with very severe hyperhidrosis may report that their QOL is not so poor because they have adapted better. All patients treated in this study reported poor or very poor QOL.

Almost all patients in good clinical condition, except those with glaucoma, can be treated with oxybutynin. This includes obese patients who might have a greater risk of compensatory hyperhidrosis after surgery and a higher surgical risk.

We used a nonobjective measurement of sudoresis in which the patients consider the amount of sweating and their daily experience instead of the objective methods.
patients become free from PH. However, this improvement, when VATS is performed, the results are even better: the therapeutic effect of oxybutynin is superior to the therapeutic effect of other procedures. Treatment of PH and AH with oxybutynin is a good initial alternative for treatment given that it presents good results and improves QOL.

**CONCLUSIONS**

The prognostic factors currently associated with a worsening of the QOL after a thoracic sympathectomy to treat hyperhidrosis are surgical failure and severe compensatory hyperhidrosis. In contrast, with clinical treatment, the use of oxybutynin is a good therapeutic alternative for the initial treatment of PH or AH. In choosing this treatment, patients have nothing to lose, and the treatment may facilitate their preparation for facing future invasive procedures. Treatment of PH and AH with oxybutynin is a good initial alternative for treatment given that it presents good results and improves QOL.

**AUTHOR CONTRIBUTIONS**

Conception and design: NW, PK, JR, PPL

Analysis and interpretation: NW, PK, JR, PPL

Data collection: NW

Writing the article: NW, PPL, PK, JR

Critical revision of the article: NW, PPL, PK, JR

Final approval of the article: NW, PPL, PK, JR

Statistical analysis: NW

Obtained funding: NW, PPL

Overall responsibility: NW

**REFERENCES**


| Table VI. Distribution of dry mouth among patients according to the dose |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Distribution    | Placebo (%)     | Placebo (%)     | Placebo (%)     | Placebo (%)     |
| Absent and mild | 15 (68.2)       | 17 (73.9)       | 20 (90.9)       | 15 (65.2)       |
| Moderate and severe | 7 (31.8)       | 6 (26.1)       | 2 (9.1)         | 8 (34.8)        |
| P(χ² test)      | .672            | .038            | .038            | .038            |

(sudorometers) that only produce data at one specific point in time. There is no method capable of measuring hyperhidrosis during an entire day. For this reason, we asked the patients to grade their improvement on a scale from 0 to 10 for each of the sites of their hyperhidrosis complaint. After all, hyperhidrosis is a disturbing—but not dangerous—disease, so the goal of any treatment is the patient’s subjective improvement.

The results after treating PH and AH with oxybutynin were satisfactory. Palmar and axillary sudoresis were decreased in >80%, and QOL improved in 74.6%. We also observed that the placebo effect (27% of moderate improvement and no big improvement) was exceedingly inferior to the therapeutic effect of oxybutynin. When VATS is performed, the results are even better: >95% of the patients become free from PH. However, this improvement is often at the cost of compensatory hyperhidrosis, an irreversible increase in sudoresis at other points of the body. Most of the patients in our study had hyperhidrosis at other sites, predominantly on the feet. An additional benefit is that the drug treatment led to a great improvement at all of the other sites with hyperhidrosis (>90% of moderate or great improvement).

Limitations of this study are the small number of patients entered into each arm of the trial, with the further reduction in patient numbers by those lost to follow-up, and the relatively short-duration study period of 6 weeks, which did not allow us to study the presence of tachyphylaxis. A larger number of patients would have given a more accurate idea about the efficiency of this medication and allowed us to separate patients with AH and patients with PH. The loss of patients is always unwelcome, but in this study, it was acceptable to be similar to other studies. Finally, a study of patients using oxybutynin for a longer period will provide an idea of how they evolve over time, and a longer follow-up will allow us to study the tachyphylaxis.

**REFERENCES**


