Effectiveness of oxybutynin for treatment of hyperhidrosis in overweight and obese patients

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ABSTRACT

Objective: Until the present moment, the lack of efficient therapeutic options available for hyperhidrosis treatment in obese patients has left this population without prospect of clinical or quality of life (QOL) improvements. Outcomes of oxybutynin treatment for overweight and obese patients with hyperhidrosis are unknown. This study aims to investigate the results related to clinical and QOL improvements in this specific population, submitted to a 12-week protocol treatment with oxybutynin.

Methods: 559 patients with palmar and axillary hyperhidrosis, routinely followed in this service, were divided into the groups, according to their body mass index (BMI) (< 25 kg/m²; 25 < BMI < 30 kg/m²; > 30 kg/m²). Improvements in QOL and in the level of hyperhidrosis were analyzed after 12 weeks of protocol treatment with oxybutynin. These parameters were investigated using a scoring system based on a scientifically validated clinical questionnaire, applied before and after treatment.

Results: 67.8% of the overweight sample group and 63% of the obese patients presented “partial” or “great” improvement in the level of hyperhidrosis. Over 65% of patients demonstrated improvement in QOL (“much better” or “slightly better”) for all three groups, with no statistical difference between them. The only adverse event associated with oxybutynin was dry mouth, observed in 63.0% of the patients.

Conclusion: Overweight and obese patients with palmar or axillary hyperhidrosis present significant improvement in QOL after treatment with oxybutynin, and the results are comparable to those of normal weight individuals.

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Eficácia da oxibutina no tratamento de hiperidrose em pacientes com sobrepeso e obesos

RESUMO

Objetivo: A falta de alternativas terapêuticas para o tratamento de pacientes obesos com hiperidrose deixa essa população sem perspectiva de melhorar suas condições clínicas e
Introduction

Hyperhidrosis is the production of excessive sweat beyond what is required for the body’s thermoregulatory needs.1 Palmar (PH), plantar (PlH), and axillary hyperhidrosis (AH) are the most frequent presentations in both genders and across all age groups. Hyperhidrosis affects approximately 3% of the general population, and actively interferes with patients’ quality of life (QOL), causing issues in social, professional, and emotional spheres.2 The psychological stress caused by excessive sweating is the main drive for patients to seek medical assistance, who are usually willing to undergo any possible treatment option that will improve their QOL. Until the present moment, the lack of efficient therapeutic options available for hyperhidrosis treatment in obese patients has left this population without prospect of improvements in QOL.

Overweight and obesity, defined as body mass index (BMI) greater than 25 kg/m^2 and 30 kg/m^2, respectively, are the main conditions associated with more severe sweating, possibly as a result of reduced heat loss due to thicker layers of fat in subcutaneous tissues. These patients have greater difficulty in maintaining normal body temperature levels, and therefore produce excessive perspiration as a compensatory mechanism.3

Video-assisted thoracic sympathectomy (VATS) is currently considered the optimal technique for treatment of primary hyperhidrosis. It is a safe, effective, and minimally invasive method;4–7 however, it presents limited applicability in obese patients. Increased surgical risk, technical limitations, and more severe levels of compensatory hyperhidrosis explain why surgical indications are greatly restricted in these individuals.8

Oxybutynin is an anticholinergic medication widely used in urology for treatment of bladder urge incontinence. Sweat glands are stimulated by acetylcholine; thus, the anticholinergic effect of oxybutynin is responsible for its effectiveness against excessive sweating.9 It is a safe medication, with few absolute contraindications; the most important is closed-angle glaucoma. Potential side effects include dry mouth, constipation, headache, nausea, and urinary retention. Few drug interactions have been reported, and when present, they involve concomitant use of cytochrome P450 metabolism-dependent medications.10,11

Recent studies have disclosed good results with the use of oxybutynin for the treatment of hyperhidrosis.12–15 Nonetheless, a specific analysis of the effectiveness of this medication in obese patients had not been conducted. This study aimed to analyze QOL after treatment with oxybutynin in obese patients with PH and AH, and to compare the results with those of normal weight individuals.

Methods

This was a retrospective study, based on medical chart review of 559 patients treated with oxybutynin from January 2007 to December 2011. The study was approved by the ethics committee of the institution.

The patients involved were divided into three groups according to their BMI. The first group was composed of 411 (73.5%) normal weight patients (BMI < 25 kg/m^2), the second consisted of 121 (21.6%) overweight patients (25< BMI < 30 kg/m^2), and the third, of 27 (4.9%) obese individuals (BMI < 30 kg/m^2).

Age, gender distribution, and location of hyperhidrosis according to BMI are shown in Table 1. The lowest average age was observed in the normal weight group. PH and female gender were predominant in all weight categories.

The same medical treatment protocol was applied to all patients. During the first week, 2.5 mg of oxybutynin were administered once a day in the evening. From the eighth to the 42nd day, the patients received 2.5 mg of the medication twice a day; from the 43rd day to the end of the 12th week, 5 mg were administered twice a day. Experience has shown that a staged administration reduces the impact of anticholinergic side effects.

Patients were analyzed in three different moments during the study. The first evaluation was performed before the start of medication; the second, after six weeks of treatment;
Table 1 – Age, site of hyperhidrosis, and gender distribution according to BMI.

<table>
<thead>
<tr>
<th>Variable</th>
<th>BMI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 25</td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td>25 &lt; BMI &lt; 30</td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td>&gt; 30</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>411</td>
<td></td>
</tr>
<tr>
<td>9-58</td>
<td>121</td>
<td></td>
</tr>
<tr>
<td>15-61</td>
<td>27</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>24.18 (±9.35)</td>
<td></td>
</tr>
<tr>
<td>24.0 (± 8.95)</td>
<td>30.0 (± 9.33)</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Site of hyperhidrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Axilar</td>
<td>185 (45.0)</td>
<td></td>
</tr>
<tr>
<td>56 (46.3)</td>
<td>17 (62.9)</td>
<td>0.059b</td>
</tr>
<tr>
<td>Palmar</td>
<td>266 (55.0)</td>
<td></td>
</tr>
<tr>
<td>65 (53.7)</td>
<td>10 (37.1)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>310 (75.4)</td>
<td></td>
</tr>
<tr>
<td>64 (52.9)</td>
<td>16 (59.2)</td>
<td>&lt; 0.001b</td>
</tr>
<tr>
<td>Male</td>
<td>101 (24.6)</td>
<td></td>
</tr>
<tr>
<td>57 (47.1)</td>
<td>11 (40.8)</td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index.

\textsuperscript{a} Student’s t-test; \textsuperscript{b} Chi-squared test.

and the last evaluation, after the completion of 12 weeks of treatment. These evaluations were used to follow-up patients’ clinical and QOL improvement. Clinical improvement was classified using a scale ranging from 0 to 10, where 0 represented no improvement, and 10 represented absence of hyperhidrosis. Clinical outcomes were ranked according to the following categories: null (from 0 to 4), partial (5 to 7), or great (8 to 10).

QOL analysis was based on a validated clinical protocol questionnaire, applied at each visit.\textsuperscript{16,17} The questionnaire was completed according to the patient’s perception of hyperhidrosis improvement, without examiners’ interference. The authors believe that self-evaluation is a reliable method for patient QOL analysis.

QOL before treatment was classified into five different satisfaction categories, calculated as the added total score from the protocol (ranging from 20 to 100). According to the scoring system, a greater score reflects a more significant impact and represents poorer QOL. When the total score was equal to or greater than \$84\$, QOL was considered “very poor”. When the total score ranged from 68 to 83, QOL was considered “poor”. Scores that ranged from 52 to 67 were considered “good”. Scores from 36 to 51 indicated “very good” results, and scores from 20 to 35 were considered “excellent”.

Similarly, improvement of QOL after treatment was also classified into five different levels. When the total was equal to or greater than \$84\$, the QOL was considered to be “worse”. When the scores ranged from 68 to 83, QOL was considered to be “slightly worse”. Scores from 46 to 58 were considered “unaltered”. Scores from 33 to 45 indicated a “slight improvement”, and scores from 17 to 32 were considered “much better”.

The following parameters were studied in both groups: progress of PH and AH, evaluation of QOL before treatment, and improvement in QOL after treatment.

Statistical analysis

The chi-squared test was performed to verify the association between categorical variables in contingency tables, and Student’s t-test was used to compare age and study group. The significance level considered for all statistical tests was 0.05.

Results

All patients enrolled in the present study classified their QOL before treatment as “poor” or “very poor”, as demonstrated in Table 2. According to the present results, obese patients considered themselves less affected by hyperhidrosis than normal or overweight individuals.

Approximately 69% of the normal BMI group classified their QOL before treatment as “very poor”, whereas over 80% of obese individuals ranked their QOL as simply “poor”. The questionnaire was re-applied after the proposed period of treatment; over 65% of patients demonstrated improvement in QOL (“much better” or “slightly better”) for all three groups, with no statistical difference between them (Table 2).

Table 3 shows clinical improvement in hyperhidrosis, according to a subjective evaluation based on the patient’s perception of his/her own symptoms. Over 60% of the patients in all groups presented partial or great improvement in the level of sweating.

The only adverse event associated with oxybutynin was dry mouth, observed in 255 cases (63.0%); however, none required discontinuation of treatment, since in most cases the symptom was classified as “light” and therefore tolerable.

Discussion

Obesity is a condition with increasing incidence and prevalence in many parts of the world, and results from an interaction of the environment, associated with genetic predisposition and overall human behavior.\textsuperscript{15} Overweight patients present increased risk of several diseases including hypertension, osteoarthritis, diabetes, certain cancers, as well as psychological disorders.\textsuperscript{18,19} Concomitant hyperhidrosis may aggravate a negative emotional state, resulting in further deterioration of overall health conditions. This reinforces the
significant need for a definitive treatment of hyperhidrosis in this specific population.

BMI is an estimation of body fat based on the ratio of a patient’s height to weight. Despite its limitations, it is one of the most commonly used anthropometric measures to assess total body adiposity, due to its simplicity, acceptable accuracy, and inexpensiveness. BMI measurements are extensively used in epidemiological studies, and are recommended as a screening tool in the initial clinical assessment of obesity. The Centers for Disease Control and Prevention defined BMI classification as follows: 1) underweight: BMI < 18.5 kg/m²; 2) normal or acceptable weight: BMI 18.5–24.9 kg/m²; 3) overweight: BMI 25–29.9 kg/m²; 4) obese: BMI > 30 kg/m². For the purpose of the present study, the relevant BMI cutoff is 25, since surgical procedures are limited in patients with BMI above this level.

Unspecific questionnaires for QOL assessment do not allow for a precise analysis of patients with hyperhidrosis, since relevant information for this disorder is not ordinarily addressed. The QOL questionnaire used in this study has been validated and used in several published documents. Its questions focus on influence of hyperhidrosis in different daily life situations, involving social, emotional, and professional activities. The higher predominance of hyperhidrosis observed in the female gender is consistent with previous studies, and can be explained by the greater concern that this condition imposes to women, leading them to seek medical assistance more often.

The group with BMI < 25 kg/m² showed a predominance of “very poor” QOL classification, higher than that observed in the other two groups. Therefore, a direct relationship between level of obesity and QOL before treatment was not clearly established in these study patients.

Improvements in hyperhidrosis after treatment were similar in all three groups, suggesting that overweight and obese patients benefit similarly to normal weight patients. This may be explained by the fact that QOL in patients with hyperhidrosis depends not only on the intensity of sweating, but also on how well the patient adapts to his/her situation. Normal weight individuals suffering with hyperhidrosis may perceive their condition as greater in severity. Excess weight patients may endure other more important worries, and therefore may give less importance to hyperhidrosis.

Reports on safety and adverse events regarding oxybutynin are based on the knowledge for treatment of urological bladder conditions. Anticholinergic side effects are the most frequent, and can occur in over 70% of patients using over 15 mg/day. The dose administered to the present patients was rather low (10 mg/day) in comparison to what is commonly used for urological purposes (15 mg/day), and this may explain the low incidence of side effects observed in this study. Dry mouth is usually benign and decreases with time of use of medication. In this study there were no reported cases of treatment interruption or discontinuation due to side effects. However, more severe and persistent side-effects can occur.

### Table 2 – Quality of life before and after treatment according to BMI.

<table>
<thead>
<tr>
<th>QOL before treatment</th>
<th>Score</th>
<th>BMI &lt; 25 n (%)</th>
<th>25 &lt; BMI &lt; 30 n (%)</th>
<th>BMI &gt; 30 n (%)</th>
<th>p&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very poor</td>
<td>84-100</td>
<td>283 (68.8)</td>
<td>41 (33.9)</td>
<td>5 (18.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Poor</td>
<td>68-83</td>
<td>128 (31.2)</td>
<td>80 (66.1)</td>
<td>22 (81.5)</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>52-67</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Very good</td>
<td>36-51</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>20-35</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>411</td>
<td>121</td>
<td>27</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3 – Improvement in hyperhidrosis after treatment.

<table>
<thead>
<tr>
<th>Treatment result</th>
<th>Score</th>
<th>BMI &lt; 25 n (%)</th>
<th>25 &lt; BMI &lt; 30 n (%)</th>
<th>BMI &gt; 30 n (%)</th>
<th>p&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>No improvement</td>
<td>0-4</td>
<td>115 (28.0)</td>
<td>39 (32.2)</td>
<td>10 (37.0)</td>
<td>0.444</td>
</tr>
<tr>
<td>Partial improvement</td>
<td>5-7</td>
<td>141 (34.3)</td>
<td>35 (28.9)</td>
<td>8 (29.6)</td>
<td></td>
</tr>
<tr>
<td>Great improvement</td>
<td>8-10</td>
<td>155 (37.7)</td>
<td>47 (38.9)</td>
<td>9 (33.4)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>411</td>
<td>121</td>
<td>27</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Chi-squared test;
<sup>b</sup> Chi-squared test comparing “unaltered” with “much better” and “slightly better”.
especially with higher doses, and may be a limiting factor for long-term use of this medication.\textsuperscript{24}

**Conclusion**

Overweight and obese patients with PH or AH reported a significant reduction in sweating and improvement in QOL after treatment with oxybutynin; the results are comparable to normal weight individuals. The use of oxybutynin in low doses should be considered as a simple and efficient therapeutic alternative to improve the QOL of these patients. Further studies are required to analyze the long-term use and safety of this medication.

**Conflict of interest**

All authors declare to have no conflict of interest.

**References**