ELSEVIER

The Use of Oxybutynin for Treating Axillary Hyperhidrosis

Nelson Wolosker,[1] José Ribas Milanez de Campos,[2] Paulo Kauffman,[1] Samantha Neves,[1] Marco Antonio Munia,[3] Fábio BiscegliJatene,[2] and Pedro Puech-Leão,[1] São Paulo, SP, Brazil

Background: To evaluate the effectiveness and patient satisfaction with the use of oxybutynin for treating axillary hyperhidrosis in a large series of patients.
Methods: One hundred two patients with axillary hyperhidrosis were treated with oxybutynin. During the first week, patients received 2.5 mg of oxybutynin once a day in the evening. From the 8th to the 42nd day, they received 2.5 mg twice a day, and from the 43rd day to the end of the 12th week, they received 5 mg twice a day. All of the patients underwent two evaluations: before and after (12 weeks) the oxybutynin treatment, using a clinical questionnaire; and a clinical protocol for quality of life (QOL).
Results: More than 80% of the patients experienced an improvement in axillary hyperhidrosis; 36.3% of them presented a great improvement, and half of the patients showed improvements at all hyperhidrosis sites. Most of the patients showed improvements in the QOL (67.5%). The patients with very poor QOL before the treatment presented greater satisfaction levels after treatment. The side effects were minor, dry mouth being the most frequent (73.5%).
Conclusions: Oxybutynin is a good alternative to sympathectomy. It presents good results and improves QOL without the side effects of sympathectomy.

INTRODUCTION

Axillary hyperhidrosis may lead patients to serious emotional disturbances.[1] Local treatment and psychotherapy have low effectiveness.[2] Injection of botulinum toxin provides good results, but only temporarily (<6 months).[3] Excision or resection of the eccrine sweat glands frequently presents low efficacy and high recurrence rates.[4] Although video-assisted thoracic sympathectomy (VATS) provides excellent resolution of axillary hyperhidrosis (90-95%).[5-7] it is associated with certain complications, of which the most frequent and most important is compensatory hyperhidrosis.[8,9] This occurs to a mild degree in most patients, but when it is severe, it may cause dissatisfaction with the procedure.[10,11]

Different anticholinergic drugs have been used in the past to treat hyperhidrosis, but because of side effects, their use has not become routine.[12]

Oxybutynin is an anticholinergic drug that can be used safely at high doses (over 15 mg/day) to treat urological disorders related to micturition.[13] One effect observed in such patients has been diminished sudoresis. Its use for treating hyperhidrosis has only been described in 3 case reports of patients with hyperhidrosis[14-16] and 1 series of 14 patients with compensatory hyperhidrosis.[17] We have observed in daily practice that oxybutynin at low doses (up to 10 mg/day) seems to generate fewer side effects, while being effective in reducing sudoresis in patients with axillary hyperhidrosis.

ClinicalTrials.gov Identifier: NCT01118429.

[1]Division of Vascular Surgery, Hospital das Clínicas, University of São Paulo Medical School, São Paulo, SP, Brazil.

[2]Department of Thoracic Surgery, Hospital das Clínicas, University of São Paulo Medical School, São Paulo, SP, Brazil.

[3]Department of Vascular Surgery, Hospital das Clínicas, University of São Paulo Medical School, São Paulo, SP, Brazil.

Correspondence to: Nelson Wolosker, MD, PhD, Division of Vascular Surgery, Hospital das Clínicas, University of São Paulo Medical School, 627 Albert Einstein Avenue, 4th Floor, Room 423, 05652-000 São Paulo, SP, Brazil, E-mail: nwolosker@yahoo.com.br

Ann Vasc Surg 2011; 25: 1057-1062
DOI: 10.1016/j.avsg.2011.06.007

Considering that the standard treatment for axillary hyperhidrosis is surgical (video-assisted thoracic sympathectomy),[18] which is often accompanied by unpleasant side effects, oxybutynin provides a possible alternative for its treatment. We anticipated that low doses of oxybutynin (up to 10 mg/day) could cause fewer side effects and could be effective in reducing the sweating in patients with axillary hyperhidrosis.

The aim of the present study was to evaluate the effectiveness of the use of oxybutynin at low doses for treating axillary hyperhidrosis in a large series of patients, and patient satisfaction with the treatment.

MATERIALS AND METHODS

This was a nonrandomized and uncontrolled study in accordance with the ethical standards of the university's Committee of Ethics for Analysis of Research Projects on Human Experimentation. From January 2007 to June 2009, 102 consecutive patients with axillary hyperhidrosis were treated with oxybutynin. Of these, 20 patients (19.6%) were lost to follow-up. Thus, data were collected from 82 patients who underwent clinical treatment. Patients with glaucoma and micturition disorders were not included.

The patients were aged between 14 and 51 years, with a mean of 28.0 ± 9.0 years and median of 23.1 years. The group was composed of 63 women (76.8%). The patients' body mass index (BMI) ranged from 16.8 to 35.5, with a mean of 23.7 ± 3.7 and median of 23.1.

In addition to axillary hyperhidrosis, 67 of these patients (83.7%) presented hyperhidrosis at other sites on the body. Palmar hyperhidrosis was observed in 39 patients (48.7%), plantar in 36 (45.0%), craniofacial in 10 (12.5%), thoracic and abdominal in 10 (12.5%), gluteal and leg in 6 (7.5%), and dorsal in 6 (7.5%). In 26 cases (32.5%), hyperhidrosis was found in association with osmidrosis.

Oxybutynin was prescribed for 12 weeks, in progressively increasing doses throughout treatment. At their first visit, the patients were given 2.5 mg of oxybutynin to be taken once a day in the evening, were instructed to increase the dose to 2.5 mg twice a day from the 8th to the 42nd day, and to contact the doctor if they experienced any side effect. After this period, they were seen in a second visit, and the dose was increased to 5 mg twice a day from the 43rd to the end of the 84th day, to when a third visit was scheduled.

All the patients underwent three evaluations for the purpose of this study: The first before the medical treatment, the second after 6 weeks, and the last after 12 weeks of oxybutynin treatment. These evaluations were used to assess (1) the patients' clinical improvement in axillary hyperhidrosis and at the other sites at which patients reported hyperhidrosis, using a clinical questionnaire; and (2) the negative impact of the condition on the quality of life (QOL), using protocol of QOL[19] that was adapted to English,[20] and the occurrence of side effects.

To evaluate the patients' improvement in hyperhidrosis, they filled out the clinical improvement questionnaire, after completion of the treatment, according to their subjective perception of improvement in sudoresis. They evaluated it on a scale from 0 to 10, where 0 represented no improvement and 10 represented 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 when the score was 0; slight, when it was 1-4; moderate, when it was 5-7; or great, when it was 8-10.

The negative impact of hyperhidrosis on QOL before the treatment was classified into five different levels, calculated as the summed total score from the protocol (range from 20 to 100). The higher the level, the greater is the impact and the poorer is the QOL. When the total was greater than 84, the QOL was considered 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 into five different evolution levels: When the total was greater than 84, the QOL was considered much worse; from 68 to 83, slightly worse; from 52 to 67, the same; from 36 to 51, slightly better; and from 20 to 35, much better.

The following parameters were studied: evolution of axillary hyperhidrosis; evolution of hyperhidrosis at other sites on the body; negative impact of hyperhidrosis in the QOL before the treatment; evaluation of improvement in QOL after the treatment; analysis of the patients' improvement in the QOL according to QOL levels before the treatment; improvement in QOL according to sex, age, and BMI; and, finally, any complications and side effects.

For categorical variables, the χ^2 or the Student *t* test was used. These statistical tests were used to compare gender, age, and BMI with the satisfaction (QOL). The associations between the improvements of QOL according to the levels before the treatment were

investigated using the McNemar test. The significance level considered for all tests was $p = 0.05$.

RESULTS

The results of the treatment related to axillary hyperhidrosis are presented in Table I.

More than 70% of the patients evolved with an improvement in axillary hyperhidrosis, and 36% of them presented a great improvement.

The results of the treatment related to other sites at which the patients had complained of hyperhidrosis are presented in Table II.

More than half of the patients showed significant improvements at all of the hyperhidrosis sites. There were no cases of worsening at other hyperhidrosis sites.

The distribution of QOL before the treatment is presented in Table III.

Before the treatment, all of the patients presented poor or very poor QOL. The median was 0.85 (±0.09).

The distribution of improvement in QOL after the treatment is shown in Table IV.

After the treatment, most of the patients presented improvements (67.5%). The median was 0.45 (±0.13).

The analysis of the evolution of QOL among the patients, according to the levels observed before the treatment, is shown in Table V.

There was an improvement in QOL following the treatment. The patients with very poor QOL before the treatment presented greater satisfaction levels after treatment.

The analysis of the evolution of QOL according to the patients' gender, age, and BMI is presented in Table VI.

There were no statistical differences in patients' evolution in relation to gender, age, or BMI.

Certain side effects were observed during the treatment. Headache was presented by two patients (3.6%) while using 5 mg of oxybutynin per day and by two patients (3.6%) while using 10 mg/day. In all cases, headache disappeared with the use of common analgesics. Urine retention was reported by a single patient while using 5 mg/day, which subsequently disappeared. Constipation was reported by six patients (7.2%) while using 5 mg/day and by five patients (6.0%) while using 10 mg/day. Suspension of oxybutynin was not necessary in any cases.

Dry mouth was the side effect most frequently reported and was present in the majority of the patients (73.5%). The distribution of this side effect is shown in Table VII.

Table I. Evolution of axillary hyperhidrosis with the use of oxybutynin

	Improvement	*n* (%)
Axillary hyperhidrosis	Worse	0 (0.0)
	Null	9 (11.2)
	Slight	14 (17.5)
	Moderate	28 (35.0)
	Great	29 (36.3)
	Total	80

Most of the patients presented some degree of dry mouth during the treatment. With higher doses, the frequency and intensity of this side effect increased.

DISCUSSION

The excellent results of sympathectomy for treating patients with hyperhidrosis, the widespread publicity of this disease in the current media, and the great incidence of this condition have led to increasing demand for treatment of this disease worldwide.[21,22] Many patients who seek medical assistance come with the preconceived idea that they need to undergo an operation, and they resist taking medications. This explains the significant number of patients among our sample who did not adhere to the clinical treatment.

Most patients are young adults, as the symptoms most frequently start during childhood.[23] Most of the patients who undergo surgery are female, and we likewise observed that the patients undergoing oxybutynin treatment were predominantly female, probably because excessive sweating has greater repercussions in women's daily lives.[24,25]

Patients using oxybutynin to treat urinary disorders take larger doses (15 mg/day) and may present more severe side effects (dry mouth, headache and urine retention).[26,27] However, we did not observe this with the low and progressive doses used in the present study. The clinical treatment used by our group is well standardized. We start the treatment with very low doses of oxybutynin (2.5 mg/day) and progressively increase the dose up to 10 mg/day. We use this protocol because patients with urinary disorders were instructed to start taking 5 mg every 12 hours and presented greater severity of dry mouth right at the beginning of the treatment. This discomfort led some patients to abandon the treatment. We found through empirical practice that by starting with very low doses (2.5 mg/day) and increasing the dose progressively (up to 10 mg/day), the incidence of side effects was lower.

Table II. Evolution of hyperhidrosis with the use of oxybutynin

	Improvement *n* (%)				
Hyperhidrosis site	Null	Slight	Moderate	Great	Total
Palmar	4 (11.1%)	1 (2.8%)	11 (30.6%)	20 (55.6%)	36
Plantar	3 (9.4)	3 (9.4)	8 (25.0)	18 (56.3)	64
Craniofacial	0 (0.0)	1 (12.5)	3 (37.5)	4 (50.0)	8
Thoracic + abdominal	1	0	1	6	8
Gluteus and legs	0	0	0	7	7
Dorsal	1	0	1	4	6
Associated osmidrosis	8 (34.8)	3 (13.0)	5 (21.7)	7 (30.4)	23

Table III. Quality of life (QOL) before oxybutynin treatment

QOL questionnaire	QOL before treatment
0.20-0.35 (excellent)	0
0.36-0.51 (very good)	0
0.52-0.67 (good)	0
0.68-0.83 (poor)	40 (50%)
0.84-1.00 (very poor)	40 (50%)

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

QOL questionnaire	QOL after treatment
0.20-0.35 (much better)	18 (22.5%)
0.36-0.51 (slightly better)	36 (45.0%)
0.52-0.67 (the same)	26 (32.5%)
0.68-0.83 (a little worse)	0
0.84-1.00 (much worse)	0

Moreover, when such effects did occur, patients were able to adapt to them better.

Dry mouth was the most frequent side effect observed. With the protocol used in this study, 83.1% of the patients either did not present dry mouth or presented it only mildly during the first phase, which encouraged the patients to continue with the treatment. With increasing doses, this symptom intensified but was well tolerated; none of the patients abandoned the treatment owing to it. Moreover, the less frequent side effects, such as slight headache, urine retention, and constipation were not a reason for the patients to discontinue the treatment.

The patients who sought medical assistance presented great dissatisfaction regarding their axillary hyperhidrosis. The degree of degradation of their QOL was measured in our study by means of a specific QOL questionnaire on hyperhidrosis,[28] which has been validated and used in several published studies.

The degree to which hyperhidrosis worsens a patient's QOL depends not only on the severity of the hyperhidrosis but also on the patient's adaptation to the condition.[29] Some individuals with less severe hyperhidrosis present very poor QOL, whereas at the other extreme, patients with very severe hyperhidrosis may report that their QOL is not so poor, because they have adapted better to their condition. All the patients treated in this sample presented poor or very poor QOL.

Practically all patients in good clinical condition, except those who present glaucoma, can be treated with oxybutynin. This includes obese patients who might present greater risk of developing compensatory hyperhidrosis and being a higher surgical risk.

We did not use any objective measurement of sudoresis because these methods only produce data at a specific point in time. There are no methods that can measure hyperhidrosis over an entire day. We asked the patients to grade their improvement on a scale from 0 to 10 for each of the sites of their complaint.

The results from treating axillary hyperhidrosis were satisfactory in that axillary sudoresis decreased in more than 70% of the cases, and in 67.1%, the results were satisfactory with regard to QOL. When surgery is performed, the results are even better, given that more than 95% of the patients become free from axillary hyperhidrosis. On the other hand, sympathectomy may give rise to compensatory hyperhidrosis, that is, an irreversible increase in sudoresis at other points of the body.[30] In the present sample, we found that almost all of the patients presented hyperhidrosis at other sites, with predominance on the hands and feet. The drug treatment indicated that there was a major

Table V. Evolution of quality of life according to the levels before the treatment

	After treatment		
Before treatment	Much better and slightly better	The same	*p* value
Poor	26 (65.0%)	14 (35.0%)	0.0426
Very poor	27 (67.5%)	13 (32.5%)	

p value obtained using the McNemar test.

Table VI. Evolution of quality of life (QOL) according to patients' gender, age, and body mass index (BMI)

Variable	Category	QOL much better + slightly better frequency (%) or measurement	QOL + the same frequency (%) or measurement	*p* value
Gender	Male	13 (68.4)	6 (31.6)	0.887
	Female	42 (66.7)	21 (33.3)	
Age (years)	*N*	55	27	0.2869[a]
	Range	13.9-51.4	15.5-44.1	
	Median	27.2	25.8	
	Mean	28.7	26.4	
	Standard deviation	10.0	6.6	
BMI	*N*	55	27	0.5493[a]
	Range	18.0-33.3	16.8-35.5	
	Median	23.2	22.4	
	Mean	23.8	23.3	
	Standard deviation	3.3	4.4	

p value obtained using the chi-squared test.
[a]*p* value obtained using the Student *t* test.

Table VII. Distribution of dry mouth among patients treated with oxybutynin

	Oxybutynin dose	
Dry mouth	5 mg	10 mg
Absent	51 (62.2%)	22 (26.8%)
Mild	17 (20.7%)	13 (15.9%)
Moderate	10 (12.2%)	22 (26.8%)
Severe	4 (4.9%)	25 (30.5%)

improvement at all the other sites of hyperhidrosis, as well as a great improvement in cases in which the patients also presented osmidrosis.

The prognostic factors currently associated with worsening of QOL following thoracic sympathectomy to treat hyperhidrosis are surgical failure and severe compensatory hyperhidrosis.[31,32] On the other hand, with clinical treatment, we did not observe any worsening of QOL. In the worst cases, QOL remained unchanged. When patients wish, the medication may be discontinued and surgical treatment may be chosen, provided that these patients are properly assisted and informed about the main side effect resulting from the surgical procedure, that is, compensatory hyperhidrosis.

From analyses of the prognostic factors for improvement of QOL through treatment with oxybutynin, we found that the patients with best results were the ones with worst QOL before the treatment. Age, gender, and BMI were unrelated to the patients' evolution.

We believe that in addition to the effectiveness presented, this therapeutic alternative is an excellent choice for the initial treatment of hyperhidrosis. It is also important to conduct a study comparing the drug with placebo.

Patients who choose this treatment have nothing to lose, and the least to be expected is that it will help prepare them to face sympathectomy in the future.

Treatment of axillary hyperhidrosis with oxybutynin represents a good alternative to sympathectomy, given that it produces good results and improves QOL, and patients do not face the risk of the side effects of sympathectomy.

Among patients undergoing oxybutynin treatment to treat primary hyperhidrosis, the worse the pretreatment QOL is, the better the postoperative improvement in QOL will be.

REFERENCES

1. Weber A, Heger S, Sinkgraven R, Heckmann M, Elsner P, Rzany B. Psychosocial aspects of patients with focal hyperhidrosis. Marked reduction of social phobia, anxiety and depression and increased quality of life after treatment with botulinum toxin A. Br J Dermatol 2005;152:342-345.
2. Stolman LP. Treatment of hyperhidrosis. J Drugs Dermatol 2003;2:521-527.
3. Grunfeld A, Murray CA, Solish N. Botulinum toxin for hyperhidrosis: a review. Am J Clin Dermatol 2009;10:87-102.
4. Hafner J, Beer GM. Axillary sweat gland excision. Curr Probl Dermatol 2002;30:57-63.
5. Munia MA, Wolosker N, Kaufmann P, de Campos JR, Puech-Leão P. Sustained benefit lasting one year from T4 instead of T3—T4 sympathectomy for isolated axillary hyperhidrosis. Clinics (Sao Paulo) 2008;63:771-774.
6. Ribas Milanez de Campos J, Kauffman P, Wolosker N, et al. Axillary hyperhidrosis: T3/T4 versus T4 thoracic sympathectomy in a series of 276 cases. J Laparoendosc Adv Surg Tech A 2006;16:598-603.
7. Munia MA, Wolosker N, Kauffman P, de Campos JR, Puech-Leão P. A randomized trial of T3-T4 versus T4 sympathectomy for isolated axillary hyperhidrosis. J Vasc Surg 2007;45:130-133.
8. de Campos JR, Wolosker N, Takeda FR, et al. The body mass index and level of resection: predictive factors for compensatory sweating after sympathectomy. Clin Auton Res 2005;15:116-120.
9. Currie AC, Evans JR, Thomas PR. An analysis of the natural course of compensatory sweating following thoracoscopic sympathectomy. Int J Surg 2011;9:437-439.
10. Cerfolio RJ, De Campos JR, Bryant AS, et al. The society of thoracic surgeons expert consensus for the surgical treatment of hyperhidrosis. Ann Thorac Surg 2011;91:1642-1648.
11. Gossot D, Kabiri H, Caliandro R, Debrosse D, Girard P, Grunenwald D. Early complications of thoracic endoscopic sympathectomy: a prospective study of 940 procedures. Ann Thorac Surg 2001;71:1116-1119.
12. Baumgartner FJ, Bertin S, Konecny J. Superiority of thoracoscopic sympathectomy over medical management for the palmoplantar subset of severe hyperhidrosis. Ann Vasc Surg 2009;23:1-7.
13. Arisco A, Brantly E, Kraus S. Oxybutynin extended release for the management of overactive bladder: a clinical review. Drug Des Devel Ther 2009;3:151-161.
14. Lefrandt JD, Maurer JM. Oxybutynin for hyperhidrosis. Neth J Med 2007;65:356.
15. Mijnhout GS, Kloosterman H, Simsek S, Strack van Schijndel RJ, Netelenbos JC. Oxybutynin: dry days for patients with hyperhidrosis. Neth J Med 2006;64:326-328.
16. Schollhammer M, Misery L. Treatment of hyperhidrosis with oxybutynin. Arch Dermatol 2007;143:544-545.
17. Tupker RA, Harmsze AM, Deneer VH. Oxybutynin therapy for generalized hyperhidrosis. Arch Dermatol 2006;142:1065-1066.
18. Moreno Balsalobre R, Moreno Mata N, Ramos Izquierdo R, et al. Guidelines on surgery of the thoracic sympathetic nervous system. Arch Bronconeumol 2011;47:94-102.
19. Amir M, Arish A, Weinstein Y, Pfeffer M, Levy Y. Impairment in quality of life among patients seeking surgery for hyperhidrosis (excessive sweating): preliminary results. Isr J Psychiatry Relat Sci 2000;37:25-31.
20. de Campos JR, Kauffman P, Werebe Ede C, et al. Quality of life, before and after thoracic sympathectomy: report on 378 operated patients. Ann Thorac Surg 2003;76:886-891.
21. Lin TS, Fang HY. Transthoracic endoscopic sympathectomy in the treatment of palmar hyperhidrosis—with emphasis on perioperative management (1,360 case analyses). Surg Neurol 1999;52:453-457.
22. Scognamillo F, Serventi F, Attene F, et al. T2-T4 sympathectomy versus T3-T4 sympathicotomy for palmar and axillary hyperhidrosis. Clin Auton Res 2011;21:97-102.
23. Gelbard CM, Epstein H, Hebert A. Primary pediatric hyperhidrosis: a review of current treatment options. Pediatr Dermatol 2008;25:591-598.
24. Araújo CA, Azevedo IM, Ferreira MA, Ferreira HP, Dantas JL, Medeiros AC. Compensatory sweating after thoracoscopic sympathectomy: characteristics, prevalence and influence on patient satisfaction. J Bras Pneumol 2009;35:213-220.
25. Nyamekye IK. Current therapeutic options for treating primary hyperhidrosis. Eur J Vasc Surg 2004;6:571-576.
26. Nabi G, Cody JD, Ellis G, Herbison P, Hay-Smith J. Anticholinergic drugs versus placebo for overactive bladder syndrome in adults. Cochrane Database Syst Rev 2006:CD003781.
27. Wang QW, Song DK, Zhang XP, et al. Urodynamic parameters development and complications of clean intermittent self-catheterization in Chinese schoolchildren with neurogenic underactive bladder. Urol Int 2011;86:461-465.
28. Sayeed RA, Nyamekye I, Ghauri AS, Poskitt KR. Quality of life after transthoracic endoscopic sympathectomy for upper limb hyperhidrosis. Eur J Surg Suppl 1998;580:39-42.
29. Lau WT, Lee JD, Dang CR, Lee L. Improvement in quality of life after bilateral transthoracic endoscopic sympathectomy for palmar hyperhidrosis. Hawaii Med J 2001;60:126-137.
30. Wolosker N, Yazbek G, Milanez de Campos JR, Kauffman P, Ishy A, Puech-Leão P. Evaluation of plantar hyperhidrosis in patients undergoing video-assisted thoracoscopic sympathectomy. Clin Auton Res 2007;17:172-176.
31. Schmidt J, Bechara FG, Altmeyer P, Zirngibl H. Endoscopic thoracic sympathectomy for severe hyperhidrosis: impact of restrictive denervation on compensatory sweating. Ann Thorac Surg 2006;81:1048-1055.
32. Bachmann K, Standl N, Kaifi J, et al. Thoracoscopic sympathectomy for palmar and axillary hyperhidrosis: four-year outcome and quality of life after bilateral 5-mm dual port approach. Surg Endosc 2009;23:1587-1593.