

Botulinum A toxin improves life quality in severe primary focal hyperhidrosis

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Focal hyperhidrosis is a condition that may disturb emotional, social and professional life. Treatment options for severe cases are surgical sympathectomy and local chemical sweat gland denervation by intradermal injections of botulinum toxin A (Btx A). The Dermatology Life Quality Index (DLQI) is a simple validated questionnaire designed to measure and compare disability in different skin diseases. The aim of this study was to assess quality of life with the DLQI before and after treatment with botulinum toxin injections in a group of patients with severe hyperhidrosis. DLQI was administered to 58 randomly chosen patients before and after treatment. All patients answered the DLQI questionnaire prior to treatment and 53/58 at mean 5.2 months after treatment. The mean DLQI score in the 58 patients before treatment was 10.3 (2-23). In the group of 16/53 patients who had a relapse of sweating when answering the DLQI a second time, no significant improvement was seen [score 10.6 before and 8.8 after treatment ($P = 0.21$)]. In patients without relapse, a 76% improvement was obtained (DLQI was reduced from 9.9 to 2.4; $P < 0.0001$). The study showed that focal hyperhidrosis may considerably reduce life quality and the disability experienced by the patients can be largely reversed by botulinum toxin injections.

Introduction

Primary focal hyperhidrosis is a common condition with excessive sweating, most often in hands, feet or axillae and more seldom in face and groins. Symptoms may give rise to serious emotional and social problems as well as functional impairment with consequences for professional life (Naver and Aquilonius, 1997). For the patients with most excessive sweating who respond poorly to conventional therapy with aluminium chloride, iontophoresis or systemic anticholinergic drugs; surgical approaches, such as transthoracic endoscopic sympathectomy (TES) or sweat gland excision of the axillae have been the next option of treatment. Several reports over the last 2 years have shown that intradermal injections of botulinum toxin A (Btx A) effectively abolish sweating in secondary focal as well as primary focal hyperhidrosis (Drobik and Laskawi, 1995; Bushara *et al.*, 1996; Naver and Aquilonius, 1997; Schneider *et al.*, 1997, 1999; Naumann *et al.*, 1998; Shelley *et al.*, 1998). The toxin acts at peripheral cholinergic nerve terminals (including sudomotor nerves) to inhibit the release of acetylcholine. Serious side-effects have not been reported since the method was introduced in 1995,

and it has therefore become an important alternative to TES and axillary surgery.

In dermatology, quality of life can be measured by disease specific, dermatology specific, general health and utility measure questionnaires (Finlay, 1997). The Dermatology Life Quality Index (DLQI) is a dermatology specific questionnaire, which can be quickly answered by the patient. The questions in the test were derived from patients with many different skin diseases. DLQI is validated using test-retesting, comparison to a control group and demonstration of change following improvement after treatment of skin diseases (Finlay and Khan, 1994). The test can be applied on all skin diseases allowing comparison with previously published DLQI scores and evaluation of change in management of skin diseases. Diseases previously studied with respect to DLQI include psoriasis/atopic dermatitis (Badia *et al.*, 1999; Linnet and Jemec, 1999; Lundberg *et al.*, 1999), acne (Newton *et al.*, 1997), urticaria (Poon *et al.*, 1999), Hailey-Hailey and Darier's diseases (Harris *et al.*, 1996) and vitiligo (Kent and Al-Abadie, 1996). The DLQI has also been used as a tool for demonstration of the impact of treatment on life quality in patients with acne (Newton *et al.*, 1997), basal cell carcinoma (Blackford *et al.*, 1996) and to in-patients with a variety of dermatological diagnoses (Kurwa and Finlay, 1995). General health measures that correlate to the DLQI include Short Form 36 (SF 36), U.K. sickness impact profile (UKSIP), and health

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state utilities (Finlay, 1997). Change in quality of life as shown by the SF 36 has previously been used with 16 patients to evaluate the influence of TES on the life quality of these patients (Sayeed *et al.*, 1998). Generic instruments measuring quality of life has also been used in patients with dystonias treated with Btx A (Gudex *et al.*, 1997, 1998).

The aim of the present study was to evaluate quality of life with the DLQI in a group of patients referred to hospital with severe hyperhidrosis and the possible improvement after treatment with botulinum toxin injections.

Materials and method

Fifty-eight patients with focal hyperhidrosis (15–49 years, 18 men and 40 women) referred to the departments of Neurology and Dermatology, from April 1998 to June 1999, were included in the study. During this 14-month period, 157 patients were referred to the clinic and the 58 patient cohort included in the study were randomly chosen. No patient refused participation. Treatment with aluminium chloride had failed in all 54 patients. Four patients had no previous treatment. One of the 58 patients had also been treated with unilateral TES, one with sweat gland excision of the axillae, six with iontophoresis, six with anticholinergic or β -blocking agents. Of the 58 patients, 46 had palmar-, 31 plantar-, and 30 axillary-localization. Eighteen had the combination of palmar and axillary hyperhidrosis and 31 palmoplantar colocalization. In total, the palms in 44 patients, the axillae in 23 and the feet in 1 (in nine the combination palms/axillae and in one palms/axillae/feet) were treated. Four of 14 patients (4/14, 29%) treated only in the axillae and 23/34 (68%) treated only in the palms also had hyperhidrosis in other sites. Intradermal injections was given with Btx A, 0.8–1 mU/cm² (Botox®, Allergan Pharmaceuticals, Irvine, CA) in glabrous skin of fingers, palms and feet and axillae after iodine starch staining. Both axillae were treated at a single visit but only one side of the palms and feet were treated at first visit and the other side 1–6 weeks later. When both hands and axillae were treated in same patient, one hand and one axilla were treated at first visit and the other hand and axilla, 1–6 weeks later. All 58 patients answered the Swedish translation of the DLQI before treatment at the department and 53/58 answered the DLQI a second time 2–13 (median 5) months after treatment, one group (18/53) replying at the follow-up visit and the other group (35/53) replying to questionnaires sent home with one reminder. Sixteen of 53 patients indicated, in the second DLQI questionnaire, that they had experienced a relapse whilst the remaining patients (37/

53) still had full or acceptable effect of the injections. Relapse was defined as subjectively unacceptable sweating. The questionnaire consists of 10 questions covering six different domains of quality of life: symptoms and feelings (questions 1 + 2), daily activities (questions 3 + 4), leisure (questions 5 + 6), work/school (question 7), personal relationships (questions 8 + 9), and treatment (question 10) (Appendix). Each answer is recorded as 0, 1, 2 or 3 giving a maximum possible score of 30 (worst possible outcome). Patients can also tick a question as 'not relevant' in which case the score for that question is 0. The score is also 0 if the patient has not replied a question. This procedure was according to the instructions for use of the scale, and only in a few cases had the patient not replied a question.

The DLQI-instrument was used with kind permission from Professor A.Y. Finlay.

Statistical analyses

Non-parametric statistics were used (Wilcoxon matched pairs test). The tests were two-tailed and *P*-values ≤ 0.05 were considered statistically significant.

Results

The mean DLQI score in the referred group of 58 patients was 10.3 (range 2–22, median 9, quartiles: 6 and 13.8) before treatment. When including all patients, with or without relapse, who answered the questionnaire two times (53/58), the DLQI score decreased from 10.1 to 4.3 ($P < 0.0001$) after treatment. During an observation time of 2–10 (median 5) months, the patients without relapse improved their index score 76% (DLQI was reduced from 9.9 to 2.4) after treatment ($P < 0.0001$). Out of 37 relapse free patients, 35 showed improved life quality after treatment according to the questionnaire. Scores in each question decreased significantly except for question 10 about treatment ($P = 0.076$; see Table 1 and Appendix). The group of eight patients treated exclusively in the axillae and without relapse improved to 79% (DLQI 11.6–2.4; $P = 0.011$; see Table 2). Twenty-one patients without relapse and with only treatment to the hands improved to 80% (DLQI 9.1–1.8; $P = 0.00019$). Scores in each of the questions decreased significantly except for question 1 about symptoms ($P = 0.14$; see Table 3 and Appendix). In the group of 16/53 patients with relapse at follow-up, the DLQI score was 10.6 before treatment and 8.8 at follow-up by at median 5 months after treatment ($P = 0.21$; see Table 4). All patients in the group with relapse had had effect of the treatment with a mean duration of 4.5 months before the relapse occurred.

Table 1 The mean values of DLQI scores in 37/58 patients free from relapse treated with botulinum toxin during a mean observation time of 4.9 (2–10) months

	Before treatment	After treatment	P-value
Mean DLQI	9.9	2.4	<0.0001
Symtoms and feelings			
Question 1	0.5	0.2	0.039
Question 2	2.1	0.6	<0.0001
Daily activities			
Question 3	0.4	0.1	0.036
Question 4	1.7	0.6	<0.0001
Leisure			
Question 5	1.5	0.2	<0.0001
Question 6	0.4	0.1	0.0086
Work, school			
Question 7	1.4	0.3	<0.0001
Personal relationships			
Question 8	1.3	0.2	<0.0001
Question 9	0.5	0.1	0.045
Treatment			
Question 10	0.4	0.1	0.076

Table 2 The mean values of DLQI scores in 8 patients only treated for axillary hyperhidrosis without relapse during a mean observation time of 4.4 (2–8) months

	Before treatment	After treatment	P-value
Mean DLQI	11.6	2.4	0.011
Symtoms and feelings			
Question 1	0.8	0.4	0.35
Question 2	2.6	0.8	0.018
Daily activities			
Question 3	0.1	0.1	–
Question 4	2.8	0.9	0.011
Leisure			
Question 5	1.2	0	0.068
Question 6	0.1	0	–
Work, school			
Question 7	1.8	0	0.011
Personal relationships			
Question 8	1.2	0.1	0.11
Question 9	0.4	0	–
Treatment			
Question 10	0.6	0.2	0.11

Areas of life quality

Questions 2, 4, 5, 7 and 8 had the most impact to the whole group of patients with hyperhidrosis. These questions cover five of six domains of quality of life, sparing only the domain of treatment. Question 4,

Table 3 The mean values of DLQI scores in 21 patients only treated for palmar hyperhidrosis without relapse during a mean observation time of 5.2 (3–10) months

	Before treatment	After treatment	P-value
Mean DLQI	9.1	1.8	0.0002
Symtoms and feelings			
Question 1	0.3	0.1	0.14
Question 2	1.8	0.5	0.0013
Daily activities			
Question 3	0.5	0	0.043
Question 4	1	0.1	0.0051
Leisure			
Question 5	1.5	0.2	0.0008
Question 6	0.5	0	0.012
Work, school			
Question 7	1.2	0.4	0.0084
Personal relationships			
Question 8	1.3	0.1	0.024
Question 9	0.7	0.1	0.0016
Treatment			
Question 10	0.3	0.1	0.024

Table 4 The mean values of DLQI scores in 16/53 patients with relapse of sweating during a mean observation time of 6.1 (2–13) months

	Before treatment	After treatment	P-value
Mean DLQI	10.6	8.8	0.21
Symtoms and feelings			
Question 1	0.4	0.2	0.11
Question 2	1.9	1.6	0.12
Daily activities			
Question 3	0.6	0.5	0.46
Question 4	1.7	1.8	0.75
Leisure			
Question 5	1.4	1.2	0.53
Question 6	0.4	0.2	–
Work, school			
Question 7	1.6	1.2	0.2
Personal relationships			
Question 8	1.6	1.1	0.055
Question 9	0.6	0.6	1
Treatment			
Question 10	0.4	0.5	0.55

which deal with dressing, gave the highest score in the subgroup where only the axillae ($n = 14$) were treated. Correspondingly, question 2 dealing with self-confidence had the highest score, i.e. gave the largest contribution to the DLQI, in the subgroup treated only in the

palms ($n = 34$) and in the whole group of 58 patients.

Discussion

The study shows that quality of life may be considerably reduced in patients with focal hyperhidrosis. In addition, the disability experienced by these patients can be largely reversed through intradermal injections with botulinum toxin. Comparisons with DLQI of other skin diseases may be carried out. The mean DLQI scores in the 58 hyperhidrotic subjects were comparable with those seen in severe acne (9.2) and pruritus (9.2 and 10.5), and higher than those seen in outpatients with psoriasis (8.9), acne (4.3), Darier's disease (5.9), Hailey-Hailey disease (6.1) and vitiligo (4.8) (Finlay and Khan, 1994; Harris *et al.*, 1996; Kent and Al-Abadie, 1996; Newton *et al.*, 1997; Sayeed *et al.*, 1998). The DLQI score from our own department in 366 out-patients with psoriasis was 5.9 and for atopic eczema 7.3 (Lundberg *et al.*, 1999).

The DLQI scores decreased to values at 1.8–2.4 and the remaining disability could possibly be explained by residual sweating from untreated areas of hyperhidrosis, e.g. the feet. We have previously reported improvement with a non-validated questionnaire in domains of mental health and social function in work and leisure (Naver *et al.*, 2000). The results correlate well to the improvement seen in this study. Our results are comparable with those from the study on acne by Newton *et al.* (1997) with regard to the patients' quality of life and the powerful improvement after treatment with systemic isotretinoin. When SF 36 was used to evaluate TES in 16 patients with palmar hyperhidrosis, a significant improvement was seen in two of eight domains, social function and mental health. We could see a significant improvement in five of six domains with DLQI in our study. Although SF 36 has been shown to correlate to DLQI for some skin diseases (Finlay, 1997), some domains in the general questionnaire do not seem relevant in patients with focal hyperhidrosis. Objective methods to visualize or weigh sweating in the patients are sometimes disappointing because the sweat rate fluctuate with time and it can be totally absent at one visit even if the patient is untreated. The patients history and subjective evaluation with the DLQI is probably a better measure of the severeness of the disease and of the effect of the treatment. DLQI was simple and practical to use, patients answered in a proper manner, and it took only a few minutes to answer. The questionnaire was sensitive to changes as seen in the relapse-free group of patients but also almost consistent in the group with relapse. The spread in follow-up time was 11 months

and was the result of practical circumstances, as late responders to the letter(s) sent home or to early late visits to the hospital. One advantage with the wide spread in follow-up time was that we could investigate patients both with and without relapse. In our trial placebo treatment was considered unethical, as it would imply regional anaesthesia of palms/feet with the potential risk of nerve damage. Furthermore, the effect of BtxA on primary focal hyperhidrosis has earlier been documented in double-blind placebo controlled studies (Schnider *et al.*, 1997, 1999). Based on the results in this study, it is concluded that treatment with intradermal injections of botulinum toxin increases the quality of life in patients with severe focal hyperhidrosis, and the treatment is recommended where conventional treatment has failed.

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DERMATOLOGY LIFE QUALITY INDEX**DLQI**

Hospital No:

Date:

Name:

Score:

Address:

Diagnosis:

The aim of this questionnaire is to measure how much your skin problem has affected your life **OVER THE LAST WEEK**. Please tick one box for each question.

- | | | | |
|-----|--|-------------------------------------|---------------------------------------|
| 1. | Over the last week, how itchy, sore, painful or stinging has your skin been? | Very much <input type="checkbox"/> | |
| | | A lot <input type="checkbox"/> | |
| | | A little <input type="checkbox"/> | |
| | | Not at all <input type="checkbox"/> | |
| 2. | Over the last week, how embarrassed or self conscious have you been because of your skin? | Very much <input type="checkbox"/> | |
| | | A lot <input type="checkbox"/> | |
| | | A little <input type="checkbox"/> | |
| | | Not at all <input type="checkbox"/> | |
| 3. | Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden? | Very much <input type="checkbox"/> | |
| | | A lot <input type="checkbox"/> | |
| | | A little <input type="checkbox"/> | |
| | | Not at all <input type="checkbox"/> | Not relevant <input type="checkbox"/> |
| 4. | Over the last week, how much has your skin influenced the clothes you wear? | Very much <input type="checkbox"/> | |
| | | A lot <input type="checkbox"/> | |
| | | A little <input type="checkbox"/> | |
| | | Not at all <input type="checkbox"/> | Not relevant <input type="checkbox"/> |
| 5. | Over the last week, how much has your skin affected any social or leisure activities? | Very much <input type="checkbox"/> | |
| | | A lot <input type="checkbox"/> | |
| | | A little <input type="checkbox"/> | |
| | | Not at all <input type="checkbox"/> | Not relevant <input type="checkbox"/> |
| 6. | Over the last week, how much has your skin made it difficult for you to do any sport? | Very much <input type="checkbox"/> | |
| | | A lot <input type="checkbox"/> | |
| | | A little <input type="checkbox"/> | |
| | | Not at all <input type="checkbox"/> | Not relevant <input type="checkbox"/> |
| 7. | Over the last week, has your skin prevented you from working or studying? | Yes <input type="checkbox"/> | |
| | | No <input type="checkbox"/> | Not relevant <input type="checkbox"/> |
| | If "No", over the last week how much has your skin been a problem at work or studying? | A lot <input type="checkbox"/> | |
| | | A little <input type="checkbox"/> | |
| | | Not at all <input type="checkbox"/> | |
| 8. | Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives? | Very much <input type="checkbox"/> | |
| | | A lot <input type="checkbox"/> | |
| | | A little <input type="checkbox"/> | |
| | | Not at all <input type="checkbox"/> | Not relevant <input type="checkbox"/> |
| 9. | Over the last week, how much has your skin caused any sexual difficulties? | Very much <input type="checkbox"/> | |
| | | A lot <input type="checkbox"/> | |
| | | A little <input type="checkbox"/> | |
| | | Not at all <input type="checkbox"/> | Not relevant <input type="checkbox"/> |
| 10. | Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time? | Very much <input type="checkbox"/> | |
| | | A lot <input type="checkbox"/> | |
| | | A little <input type="checkbox"/> | |
| | | Not at all <input type="checkbox"/> | Not relevant <input type="checkbox"/> |

Please check you have answered EVERY question. Thank you.

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