Patient-reported Outcomes and Clinical Response in Patients with Moderate-to-severe Plaque Psoriasis Treated with Tonsillectomy: A Randomized Controlled Trial

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Psoriasis is a chronic inflammatory skin disease with profound effects on patients' health-related quality of life (HRQoL). Twenty-nine patients with plaque psoriasis and a history of streptococcal-associated psoriasis exacerbations were randomly assigned to tonsillectomy (n = 15) or control (n = 14) groups and followed for 24 months. Patients were evaluated with the Psoriasis Disability Index, Psoriasis Life Stress Inventory and Psoriasis Area and Severity Index. HRQoL and psoriasis-related stress improved significantly in the tonsillectomy group compared with the control group (p = 0.037 and p = 0.002, respectively), with a mean 50% improvement in HRQoL and a mean 59% improvement in psoriasis-induced stress. Clinical improvement correlated significantly with improved HRQoL (r = 0.297, p = 0.008) and psoriasis-related stress (r = 0.310, p = 0.005). Of the tonsillectomized patients, 87% concluded that the procedure was worthwhile. Tonsillectomy may improve quality of life for selected patients with plaque psoriasis.

Key words: chronic plaque psoriasis; streptococcal throat infection; tonsillectomy; health-related quality of life; Psoriasis Disability Index; Psoriasis Life Stress Inventory.

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Psoriasis is a complex multifactorial disease caused by a combination of genetic and environmental factors (1), affecting approximately 2–3% of the world’s population (2). Psoriasis has a significant negative impact on many areas of health-related quality of life (HRQoL), including physical, occupational, social, psychological, and sexual wellbeing (3–5). Patients with psoriasis have skin-homing T cells that recognize homologous streptococcal M-protein and skin keratins (22). We report here findings related to patient HRQoL and psoriasis-induced stress and their association with clinical improvement after tonsillectomy.

METHODS

Patients

Patient eligibility criteria have been detailed previously (22). Briefly, eligible patients were ≥ 18 years of age; had moderate-to-severe chronic plaque psoriasis diagnosed by a dermatologist; had a history of sore throat-associated psoriasis exacerbation; and were willing to undergo tonsillectomy. Exclusion criteria were: underlying medical conditions, such as heart and lung diseases and bleeding disorders; alcohol or drug abuse; pregnancy; and previous tonsillectomy. Before study initiation patients were required to discontinue all psoriasis treatment except moisturizers within the previous 4 weeks.

Fifty-four patients were screened for the study, the majority of whom were referred by a dermatologist (44%) or responded to an advertisement (46%). A few patients had heard about the study by other means (6%) or were referred by an otolaryngologist (4%). Written informed consent was obtained from each patient before initiation of study participation. A total of 29 patients met the inclusion criteria.

Study design

This was a single-centre, 24-month, parallel, assessor-blind, randomized controlled trial. Data were collected within the de-
Psoriasis-related stress was assessed with the Psoriasis Life Stress Inventory (PLSI) (24). The PLSI is a 15-item questionnaire that estimates psychosocial stress due to psoriasis. For each question the patients must rate the level of stress experienced over the previous 4 weeks on a 4-point scale, ranging from “not at all” to “very much.” The PLSI score, ranging from 0 to 45, is calculated by summing the scores for each question. Both the PDI and PLSI have been used in the English version for evaluation of psoriasis.

Moreover, the questions were translated into Icelandic using the translation-back-translation procedure and validated by the Nordic Quality of Life study (25). The patients completed both questionnaire at study entry and at 12 and 24 months.

After the 24-month study period, participants answered a study-specific questionnaire with the aim of rating the overall experience of having tonsillectomy as a treatment for psoriasis. The questionnaire was composed of 20 multiple-choice questions, rated on a scale ranging from “not at all” to “very much” and 3 short-answer questions. The questions addressed difficulties associated with the tonsillectomy, recovery time, complications, and whether the operation had been worthwhile. Also, questions about self-perceived improvement in psoriasis, psoriasis nails and/or psoriatic arthritis and regarding HRQoL and psoriasis stress.

Clinical evaluation

Clinical follow-up has been detailed previously (22). Briefly, clinical severity was assessed by PASI score (10) at study entry and at 2, 6, 12, 18 and 24 months. The use of psoriasis treatments, such as moisturizers, topical treatments or systemic therapy, and if they had experienced sore throat or streptococcal throat infections with subsequent exacerbation of psoriasis after removal of their tonsils.

Statistical analysis

Patient demographics were summarized descriptively and data were tested for normality using the Kolmogorov-Smirnov test. PDI and PLSI scores at months 12 and 24 were compared between the groups and with baseline scores using an analysis of variance (ANOVA) test for repeated measurements. Data for months 12 and 24 were analysed with the intent-to-treat method, where any missing data were replaced using the last observation carried forward (LOCF) method. Square root transformation of the results

Table 1. Demographic data for the 29 participating patients with psoriasis

<table>
<thead>
<tr>
<th></th>
<th>Tonsillectomy group (n = 15)</th>
<th>Control group (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men, n (%)</td>
<td>3 (20)</td>
<td>6 (43)</td>
</tr>
<tr>
<td>Age, years, mean ± SD</td>
<td>35.3 ± 9.9</td>
<td>35.9 ± 9.8</td>
</tr>
<tr>
<td>BMI (kg/m²), mean ± SD</td>
<td>25.2 ± 5.3</td>
<td>25.4 ± 3.6</td>
</tr>
<tr>
<td>Smokers, n (%)</td>
<td>4 (27)</td>
<td>6 (43)</td>
</tr>
<tr>
<td>Age at psoriasis onset, years, mean ± SD</td>
<td>15 ± 7.9</td>
<td>15 ± 7.1</td>
</tr>
<tr>
<td>Sore throat psoriasis onset, n (%)</td>
<td>3 (20)</td>
<td>2 (14)</td>
</tr>
<tr>
<td>Duration of psoriasis, years, mean ± SD</td>
<td>19.9 ± 9.5</td>
<td>20.5 ± 11.7</td>
</tr>
<tr>
<td>Psoriasis family history, n (%)</td>
<td>12 (80)</td>
<td>12 (86)</td>
</tr>
<tr>
<td>Psoriatic arthritis, n (%)</td>
<td>4 (27)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>PASI score, mean ± SD</td>
<td>11.0 ± 5.7</td>
<td>9.3 ± 3.7</td>
</tr>
<tr>
<td>PDI score, mean ± SD</td>
<td>10.4 ± 7.1</td>
<td>9.3 ± 7.3</td>
</tr>
<tr>
<td>PLSI score, mean ± SD</td>
<td>12.0 ± 6.1</td>
<td>10.0 ± 7.0</td>
</tr>
<tr>
<td>Previous treatments, n (%)</td>
<td>8 (53)</td>
<td>8 (57)</td>
</tr>
<tr>
<td>Topical agents</td>
<td>5 (33)</td>
<td>4 (29)</td>
</tr>
<tr>
<td>Phototherapy</td>
<td>1 (7)</td>
<td>0</td>
</tr>
</tbody>
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SD: standard deviation; BMI: body mass index; PASI: Psoriasis Area and Severity Index, PDI: Psoriasis Disability Index, PLSI: Psoriasis Life Stress Inventory.
was used to better approximate normality in the ANOVA model. Statistical significance was defined by \( p < 0.05 \). Spearman’s rank correlation analysis was performed to evaluate the relationships between clinical improvement and improvement in HRQoL (PDI and PLSI scores) from baseline to month 24. Data analyses were performed using R software, version 2.10 (The R foundation, Austria).

**RESULTS**

Of the 54 patients with psoriasis who were screened, 38 met all the inclusion criteria. Six eligible patients were excluded due to chronic disease, ongoing systemic psoriasis treatment and pregnancy, and 3 declined to participate after screening. Thus, a total of 29 patients with plaque psoriasis and a history of psoriasis exacerbation during or after a sore throat were enrolled in the study (Fig. 1). Fourteen patients in the tonsillectomy group and 12 in the control group completed the 24-month follow-up, which took place from November 2008 to January 2011. One patient in the tonsillectomy group was started on methotrexate to treat his psoriatic arthritis after 12 months of participation. Two patients in the control group did not complete the study, one was diagnosed with lymphoma after 12 months, and the other violated the protocol by having tonsillectomy after 18 months of follow-up. There were no clinically meaningful differences between the groups and, although the tonsillectomy group had slightly higher baseline PASI, PDI and PLSI scores compared with the control group, these differences were not statistically significant (Table I).

There was a significant improvement in HRQoL after tonsillectomy (Fig. 2A). The mean PDI score decreased significantly in the tonsillectomized group, both with time (\( p = 0.026 \)) and compared with the controls (\( p = 0.037, 95\% \) confidence interval (CI) 1.43–3.58). No corresponding changes were observed for the control group. Panel B: Tonsillectomized patients reported less daily stress associated with their psoriasis, which was reflected in significantly decreased Psoriasis Life Stress Inventory (PLSI) score, both with time (\( p < 0.001 \)) and compared with the controls (\( p = 0.002, 95\% \) CI 1.39–3.10). The control group observed no corresponding changes. TX: tonsillectomy group. *Statistical significance.

![Fig. 2](image-url) Changes in health-related quality of life (HRQoL) and psoriasis-induced stress of the 29 participating psoriasis patients during the 24-month follow-up. Panel A: Tonsillectomized patients reported an improvement in HRQoL with a significant decrease in the mean Psoriasis Disability Index (PDI) score, both with time (\( p = 0.026 \)) and compared with the controls (\( p = 0.037, 95\% \) confidence interval (CI) 1.43–3.58). No corresponding changes were observed for the control group. Panel B: Tonsillectomized patients reported less daily stress associated with their psoriasis, which was reflected in significantly decreased Psoriasis Life Stress Inventory (PLSI) score, both with time (\( p < 0.001 \)) and compared with the controls (\( p = 0.002, 95\% \) CI 1.39–3.10). The control group observed no corresponding changes. TX: tonsillectomy group. *Statistical significance.

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<th>Table II. Mean changes in domains of the Psoriasis Disability Index (PDI) before and after tonsillectomy of the 29 participating patients with psoriasis</th>
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<tbody>
<tr>
<td><strong>PDI change at 12 months</strong></td>
</tr>
<tr>
<td><strong>Tonsillectomy</strong> Mean ± SD</td>
</tr>
<tr>
<td>Daily activity</td>
</tr>
<tr>
<td>Work/school</td>
</tr>
<tr>
<td>Relationships</td>
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<tr>
<td>Leisure</td>
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<td>Treatment</td>
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ns: non-significant; SD: standard deviation.
significant positive correlation between improvement in PASI score and improved psoriasis-related stress ($r=0.310, p=0.005$) (Fig. 3B).

At the end of the study, all the patients who had tonsillectomy answered a short, study-specific, questionnaire. Twelve (80%) patients felt that the surgery had been quite difficult and that the recovery took more time than they had expected. No major post-operative complications were reported, but one patient had minor bleeding the day after the procedure. Nevertheless, 13 (87%) of the patients thought that the surgery was worthwhile, and 80% reported that the procedure was worthwhile, and 80% reported being an overall difficult procedure to go through, leads to a significant positive impact on the activities of daily life and psychosocial wellbeing of patients. Thus, the HRQoL improved by 50% and tonsillectomized patients reported almost 60% lower psoriasis-related stress after the surgery. One out of 4 patients who had concomitant psoriasis arthritis reported an improvement in arthritis after the tonsillectomy.

**DISCUSSION**

We and others (22, 27, 28) have previously reported that tonsillectomy can have marked clinical benefits for selected patients with psoriasis. We now extend these findings to demonstrate that the improvement in clinical activity of psoriasis achieved through tonsillectomy, despite being an overall difficult procedure to go through, leads to a significant positive impact on the activities of daily life and psychosocial wellbeing of patients. Thus, the HRQoL improved by 50% and tonsillectomized patients reported almost 60% lower psoriasis-related stress after the surgery. Furthermore, we found that the increased HRQoL and improved psoriasis-related stress correlated positively with the observed clinical improvement, as assessed by PASI scores.

Patients with psoriasis have a 10-fold higher frequency of symptomatic streptococcal throat infections than matched household controls (14), and the asymptomatic carrier rate for group A, C and G Streptococci has been reported to be as high as 44% in patients with plaque psoriasis and a known history of psoriasis exacerbation associated with sore throat (29). Furthermore, up to 70% of Icelandic patients with plaque psoriasis report an exacerbation of psoriasis symptoms during streptococcal throat infections (30). Thus, the genetic background of patients with psoriasis appears to be permissive for both streptococcal carriage and symptomatic streptococcal throat infections, and the latter has long been associated with flares of guttate psoriasis (12, 15, 31) as well as worsening of chronic plaque psoriasis (13, 14). It would be of interest to measure antistreptolysin O (ASO) titres (32) in patients who have tonsillectomy and correlate titres with both clinical improvement and increased HRQoL. We have recently reported that patients who benefit most from tonsillectomy, both clinically and in terms of quality of life, significantly more often have psoriasis onset associated with a throat infection. Furthermore, these patients reported an increased frequency of streptococcal throat infections per lifetime and were carriers of both copies of *HLA-Cw*<sup>0602</sup> (33). The mechanism whereby *HLA-Cw*<sup>0602</sup> predisposes to psoriasis is currently unknown. Our data, and those of others (17, 34–37), are consistent with the hypothesis that autoantigens presented in the binding pockets of *HLA-Cw*<sup>0602</sup> on epidermal cells are recognized by CD8<sup>+</sup> T lymphocytes infiltrating lesional epidermis (18).

Although not yet validated, our end-of-study questionnaire gave an insight to the experience of having tonsillectomy to treat plaque psoriasis. Despite the risk of having the surgery, risk of post-operative complications and prolonged recovery time, 87% of the patients thought that the procedure was worthwhile, and 80% reported a marked improvement, which is concordant with the
recorded reduction in PASI scores, ranging from 30% to 90%, in 87% of patients (22). Furthermore, 80% of the patients reported that their need for psoriasis treatment in the form of moisturizers, topical treatments, ultraviolet light treatment or other treatments was noticeably less after the tonsillectomy. This is in accordance with our previous finding that patients with plaque psoriasis needed less symptomatic treatment after tonsillectomy compared with controls (22).

One out of the 4 patients with concomitant plaque psoriasis and psoriatic arthritis (PsA) reported at the end of the study that his arthritis had improved after the tonsillectomy. Interestingly, this patient was homozygous for HLA-Cw*0602, which is strongly associated with cutaneous psoriasis (38, 39), early onset psoriasis (40–42), and psoriasis exacerbations after streptococcal throat infection (43, 44). There are very few studies that have explored a possible link between PsA, the tonsils and streptococcal throat infections. DNA encoding the 16S ribosomal RNA gene of group A streptococci has been found in the blood and synovial fluid of patients with PsA (45), and synovial T cells from patients with PsA have been reported to respond to streptococcal superantigens, but not to conventional streptococcal antigens (46).

There is currently no cure for psoriasis, and available treatments only offer symptomatic relief, as psoriasis typically relapses when treatments are discontinued. Our results suggest that selected patients with plaque psoriasis and a history of sore throat-associated exacerbation could benefit from tonsillectomy, both with respect to clinical measures of disease severity (PASI) as well as improved quality of life and reduced disease-related stress. Although our patient cohort was followed for only 2 years, we have observed that the improvement remains at least 5 years post-tonsillectomy (unpublished data). We therefore conclude that tonsillectomy may be a significant addition to the current psoriasis treatment for a selected patient group, and offer a long-lasting improvement. However, more robust trials and long-term follow-up of tonsillectomized patients with plaque psoriasis are needed.

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The authors declare no conflicts of interest.

REFERENCES


