Topical clindamycin versus systemic tetracycline in the treatment of hidradenitis suppurativa

Gregor B. E. Jemec, MD, DMedSci, a and Peter Wendelboe, MD ∗ Copenhagen and Århus, Denmark

Background: Antibiotics are often used to treat hidradenitis, but only topical clindamycin has been shown to be effective in a randomized controlled trial. The paucity of these trials may be the result of difficulties in disease assessment.

Objective: We compare topical clindamycin with systemic tetracycline in the treatment of hidradenitis suppurativa, and study clinical disease assessment.

Methods: A total of 46 patients with stage 1 or 2 hidradenitis suppurativa were treated in a double-blind, double dummy controlled trial.

Results: No significant difference was found between the two types of treatment. Patients’ global assessment of disease was significantly worse than physician’s assessment in 3 of 5 evaluations (P = .0096 to .015), but the correlation between patients’ and physicians’ assessments was satisfactory after only one visit (rs = .761 to .895). Soreness was the key factor in patients’ overall assessment of the disease.

Conclusion: Systemic therapy with tetracyclines did not show better results than topical therapy with clindamycin. Subjective factors, particularly soreness, appear to be a key factor in patients’ assessment of the disease and should, therefore, be included as an outcome variable in future therapy studies.

(J Am Acad Dermatol 1998;39:971-4.)

Different types of antibiotic therapy are commonly used in the treatment of hidradenitis suppurativa although viable bacteria are only found in approximately 50% of all lesions.1,2 Only topical clindamycin has, however, been tested in a randomized controlled trial (RCT) in a study by Clemmensen.3 To our knowledge, the efficacy of other antibiotics has never been shown in an RCT.

Clinically relevant and objective disease assessment is a prerequisite for rational studies of therapy, and no standard disease assessment in hidradenitis exists. Hurley4 has proposed a staging of the disease that is of great general value, but focuses on elements such as scarring and sinus tract formation. These are long-term changes and may, therefore, not be sufficiently dynamic for outcome analysis in shorter clinical trials.

We have conducted an RCT based on the previously published trial, and compared the clinical efficacy of topical clindamycin against that of systemic tetracycline focusing on the disease assessment in an attempt to provide a better criteria for future trials in hidradenitis.

MATERIALS AND METHODS

The protocol was approved by the local Ethics Committee for Copenhagen. Patients were recruited from those referred for treatment or patients in whom hidradenitis suppurativa was an incidental finding on physical examination. After informed consent was obtained, a total of 46 patients (39 women and 7 men) with hidradenitis suppurativa were included in the study. A group of 12 patients were not available for evaluation (7 did not show up for scheduled visits, 2 discontinued treatment because of gastrointestinal upset, and 1 each because of lack of effect, concomitant treatment with another antibiotic, and suspected allergic reaction to topical medication).

The characteristics of the patients who completed the study are given in Table I. Treatments were compared in a double-blind double dummy study by means of parallel groups and computerized blinded randomization. Uniform containers, placebo tablets, and placebo lotion were provided by the Upjohn Company. After
informed consent was obtained, consecutive patients with early-stage (Hurley stage 1 or 2: single abscesses without sinus tracts, or recurrent but widely separated lesions with sinus tracts and scarring) hidradenitis suppurativa were assigned according to the prerandomized sequence of treatments. Dropouts were replaced, and appropriate additional medication was delivered without breaking the double-blind design of the study.

Pregnant or breast-feeding mothers were not included. Additional clinical exclusion criteria were acne conglobata (active disease on convex areas of the body); signs of staphylococcal infection; staphylococcosis; treatment with a systemic or topical antibiotic within the past 7 days; known or suspected hypersensitivity to tetracycline, lincosamides, or any constituents of the medication or placebo given; signs of systemic infection; history of impaired renal or liver function; known severe underlying disease; treatment with steroids within the past 7 days; chronic bowel diseases or diarrhea; treatment with cyproterone acetate within the past 6 months; and more than 10 lesions (nodules/abscesses) from all sites together or Hurley stage 3 (diffuse involvement, multiple interconnected abscesses, and multiple sinus tracts).

Before treatment an aseptic aspiration was taken from inflamed lesions. If aspiration was not directly possible 0.5 mL of isotonic saline was injected and aspirated. The bacteriologic analyses have been described in detail elsewhere.2

All patients received a minimum of 3 months of therapy with systemic as well as topical treatment, that is, active systemic plus topical placebo, or systemic placebo plus active topical. Active systemic treatment consisted of tetracycline 1 g daily, taken as two 250 mg capsules twice daily. Active topical treatment consisted of 1% clindamycin phosphate (Dalacin T, Upjohn Co) in a vehicle of propylene glycol, isopropyl alcohol, and water, applied twice daily.

Patients were seen monthly for evaluation of the following outcome variables: patient global evaluation on 100 mm Visual Analogue Scale (VAS) score, soreness evaluation on 100 mm VAS score, physician global evaluation on 100 mm VAS score, counting of abscesses, and counting of nodules.

The results were assessed by means of analysis of variance and a Wilcoxon 2-sample test for change from the baseline. The results of assessment were compared by means of Spearman correlations and stepwise regression analysis. Results were reported with median values and 95% confidence interval (CI).

**RESULTS**

No significant differences were found between the two treatments, but significant changes occurred in the course of the study (Figs 1 and 2). The presence of bacteria at the onset of treatment did not affect the outcome.

Significant correlations were found between disease features. Patients assessed the disease as significantly worse than physicians in 3 of 5 evaluations ($P = .0096$ to $P = .015$). Stepwise regression revealed that soreness and nodules were significantly correlated with the patients’ overall evaluation at the first visit, whereas soreness, abscesses, and the physicians’ overall evaluation were significantly correlated at the last visit. For the physicians the number of abscesses was significantly correlated with the overall disease assessment at the first visit, whereas the patients’ overall assessment appeared to be the only factor significantly associated with the physicians’ overall evaluation at the last visit.

There was a significant correlation between patients’ and physicians’ global assessment of the disease at every session (all $P < .001$; $rs = .551$ [baseline], $rs = .762$ [4 weeks], $rs = .836$ [8

### Table I. Baseline data about the patients enrolled, given as median and 95% confidence intervals

<table>
<thead>
<tr>
<th></th>
<th>Systemic treatment group</th>
<th>Topical treatment group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No. of patients enrolled</td>
<td>24</td>
<td>22</td>
</tr>
<tr>
<td>Age (y)</td>
<td>31.8 (27.3-36.5)</td>
<td>33.3 (28.9-37.8)</td>
</tr>
<tr>
<td>Drop-outs</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Sex of evaluated patients (M/F)</td>
<td>3/13</td>
<td>3/15</td>
</tr>
<tr>
<td>Patient assessment at baseline</td>
<td>35.9 (20.4-51.5)</td>
<td>48.0 (31.5-64.5)</td>
</tr>
<tr>
<td>Physician assessment at baseline</td>
<td>31.6 (19.1-44.0)</td>
<td>25.7 (13.6-37.8)</td>
</tr>
<tr>
<td>Nodules at baseline</td>
<td>2.5 (1.2-3.8)</td>
<td>2.9 (1.6-4.2)</td>
</tr>
<tr>
<td>Abscesses at baseline</td>
<td>1.9 (1.2-2.5)</td>
<td>0.8 (0.1-1.4)</td>
</tr>
<tr>
<td>Scarring at baseline (% of area)</td>
<td>45.2 (12.9-77.5)</td>
<td>27.8 (0-58.1)</td>
</tr>
<tr>
<td>Total number of adverse events in group</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>
DISCUSSION

Antibiotics are commonly used in early-stage hidradenitis, although the evidence for their efficacy is limited. Several case reports and open studies exist, but the only RCT of antibiotics describes the effect of topical clindamycin. Topical clindamycin was therefore compared with systemic tetracycline. No significant differences were seen between the two treatments.

Two types of lesions were described: abscesses and nodules. Abscesses were reduced during the first 3 months of treatment. Nodules, on the other hand, only appeared to be reduced in number after 3 months of treatment. The time course suggests that nodules may be precursors to abscesses, as previously suggested by epidemiologic studies.

A progressive improvement was noticed in subjective overall assessment and physician assessment, although soreness did not appear to change during the course of the study. The variation in individual pain thresholds may be important in coping with hidradenitis. Coping and patients’ general assessment of disease intensity for skin diseases is also influenced by factors other than the
diagnosis itself. One of these may be the visibility of the lesions in normal social intercourse. Previous studies have suggested that acne patients with facial acne cope better than patients with predominantly truncal acne because no support or sympathy is elicited by hidden lesions. This mechanism may be relevant in hidradenitis, and may explain some of the difference in the overall assessment of the disease by patients and physician. The impact of professional knowledge on the physician’s assessment also is involved. A previous study suggested that the impact of medically “benign” diseases on quality-of-life may be underestimated by the physician, whereas medically “malignant” diseases (eg, generalized connective tissue diseases or frank malignancy) are often underestimated by the patients.

In the assessment of congruity between the different outcome variables studied, two key points were noticed. First, patients and physicians considered different points important, and second, overall agreement improved in the course of the trial.

The most important factor in the patients’ overall assessment of disease severity appears to be soreness. This is in good accordance with previous studies. In lieu of true objective measures of disease activity in hidradenitis suppurativa it is, therefore, suggested that standard clinical outcome variables are supplemented with records of the patients’ subjective assessment of pain and overall disease activity.

Second, an increased consensus between patients’ and physicians’ assessment of the disease was observed at the end of our study. The correlation coefficient at baseline was only 0.551, whereas it was 0.762 at the visit only 4 weeks later. This suggests that a mutual learning process takes place and that this type of soft data gains validity as studies become longer. These observations suggest that the duration of future studies on early hidradenitis should not contain less than 3 visits at 1-month intervals.

REFERENCES