Increased Doses of Adalimumab are Associated With Clinical Improvement of Hidradenitis Suppurativa

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ABSTRACT

Background: TNF-inhibitor adalimumab 40 mg/week (ADA40) is the only approved treatment for hidradenitis suppurativa (HS); however, it is not uniformly effective. Despite a high prevalence of comorbid obesity in HS patients, adalimumab dosing is not weight-based, unlike other TNF-inhibitors.

Objective: To evaluate the effectiveness of adalimumab 80 mg/week (ADA80) compared with ADA40 in overweight and obese patients with moderate to severe HS.

Methods: We conducted a dual-center retrospective chart review of HS patients treated with ADA80 between August 2016 and December 2021. We collected data on demographics, comorbidities, treatments, and disease severity that are presented as descriptive statistics and compared with Wilcoxon signed-rank test.

Results: Eight patients with median body mass index of 36.6 (IQR 32.5–40.7) and no improvements in HS severity on ADA40 were prescribed ADA80. Patients experienced improved HS-Physician Global Assessment (ADA40: median 3.0 (3.0-3.8); ADA80: (2.0 (1.8, 2.0)) (P=0.01)), all 5 patients who had lesion counts documented achieved HS Clinical Response, and all 8 patients reported symptom improvements.

Conclusions: Increased adalimumab dose may be associated with improved outcomes for overweight and obese patients with moderate to severe HS.

J Drugs Dermatol. 2023;22(6):615-617. doi:10.36849/JDD.6868

INTRODUCTION

Hidradenitis suppurativa (HS) is a debilitating chronic inflammatory disease with a single approved treatment, TNF-antagonist adalimumab 40 mg/week (ADA40). However, only half of patients treated with ADA40 achieved Hidradenitis Suppurativa Clinical Response (HiSCR) in phase 3 trials.[1] We suspect that the limited effectiveness of this drug may be affected by inadequate dosing. HS patients are 4-times more likely to be obese than the general population, however, unlike other TNF-inhibitors, adalimumab dosing is not weight-based.[1,2] In this study, we evaluated the effectiveness of adalimumab 80 mg/week (ADA80) in 8 overweight and obese HS patients with ADA40-refractory disease.

MATERIALS AND METHODS

In this dual-center retrospective cohort study, patients seen between August 2016 and December 2021 with an ICD-10 code for HS and treated with ADA40 were screened for dose escalation to ADA80. Patients were included if they had a Hurley or HS-Physician Global Assessment (HS-PGA) score indicating moderate or severe HS, had a BMI >25, and were treated with ADA80 for at least 3 months. Data were collected on demographics, comorbidities, treatments, adverse events, patient-reported symptoms, and HS severity (HS-PGA and HiSCR) at ADA40 and ADA80 (Table 1). We report descriptive statistics and comparisons using Wilcoxon signed-rank test. This study was approved by the University of California, San Francisco Institutional Review Board (IRB) and did not require approval from the Kaiser Permanente Northern California IRB.

RESULTS

Eight patients (6 female, 2 male) from diverse racial backgrounds (5 Black, 2 White, and one multiracial: White and Asian) were included in the study. At the time of dose escalation from ADA40 to ADA80, median age was 37.0 years (25.5-41.5), and median BMI was 36.6 (32.5-40.7). Median follow-up on ADA40 was 11.2 months (9.3-20.1), and 13.2 months (3.7-27.2) on ADA80.

TABLE 1.

Patient Characteristics, Disease Severity, and Concomitant Medications During Treatment With ADA40 and ADA80		
Total patients, n	8	
Female sex, n (%)	6 (75.0%)	
Age, y (median, IQR)	37.0 (25.5-41.5)	
BMI, kg/m² (median, IQR)	36.6 (32.5-40.7)	
Race/ethnicity, n (%)		
White	2 (25.0%)	
Black	5 (62.5%)	
Mixed race†	1 (12.5%)	
Comorbidities, n (%)		
Mood disorders	3 (37.5%)	
Diabetes‡	4 (50.0%)	
Dyslipidemia	1 (12.5%)	
Hypertension	4 (50.0%)	
Pilonidal sinus	2 (25.0%)	
Psoriasis	2 (25.0%)	
Tobacco smoking	3 (37.5%)	
Treatment	ADA40	ADA80
Treatment duration, mo. (median, IQR)	11.2 (9.3-20.1)	13.2 (3.7-27.2)
Affected sites, n (%)		
Axilla	7 (87.5%)	7 (87.5%)
Gluteal and perineal regions	6 (75.0%)	4 (50.0%)
Groin	7 (87.5%)	8 (100.0%)
Other§	3 (37.5%)	1 (12.5%)
Concomitant treatments, n (%)		
Systemic antibiotics	7 (87.5%)	4 (50.0%)
Methotrexate	1 (12.5%)	1 (12.5%)
Surgery	0 (0.0%)	2 (25.0%)
Other¶	1 (12.5%)	2 (25.0%)
HS-PGA (median, IQR)*	3.0 (3.0-3.8)	2.0 (1.8-2.0)
HiSCR achieved, n (%)	0/2 (0.0%)	5/5 (100.0%)
Patient-reported symptom improvement, n (%)		
Pain	N/A	5 (62.5%)
Drainage	N/A	4 (50.0%)
Flare frequency and duration	N/A	5 (62.5%)
New lesions	N/A	4 (50.0%)

†One patient identified as White and Asian
‡Diabetes includes one patient with gestational diabetes and one patient with pre-diabetes
§Other affected sites on ADA40 include one person each with involvement of the infra-abdominal fold, posterior neck, and retro-auricular crease, and on ADA80 includes one person with infra-abdominal fold involvement
¶Other concomitant medications on ADA40 include 1 person treated with spironolactone, and on ADA80 include one person on spironolactone and another person with comorbid diabetes on metformin
*Statistically significant difference, P= 0.01

Disease improvement was not observed on ADA40 in any of the 6 patients for whom pre-ADA40 data were available (pre-ADA40: median HS-PGA 3.0 (3.0-3.0); ADA40: HS-PGA 3.0 (3.0-3.8), P=0.08); HiSCR was not achieved in the 2 patients for whom lesion counts were available). At time of dose escalation, all patients had recurrent and new inflammatory lesions, pain, and drainage on ADA40.

On ADA80, patients experienced one-point reduction in median HS-PGA (2.0 (1.8-2.0), P=0.01). HiSCR was achieved in all 5 patients for whom lesion counts were available. All patients reported improvement in HS symptoms, including reduced pain, drainage, lesions, and frequency and duration of flares on ADA80. No adverse events were reported with ADA80.

DISCUSSION

We report improved median HS-PGA and patient-reported symptomatology in response to ADA80 treatment in overweight and obese patients with moderate-to-severe HS who failed to respond to ADA40. It is noteworthy that two patients achieved sufficient disease improvement on ADA80 to become eligible for definitive surgical management.

Obesity is commonly associated with HS. Obese patients who are prescribed TNF-inhibitors for immune-mediated inflammatory diseases are more likely to fail treatment than non-obese patients.[7] It is yet to be determined if treatment failure is due to inadequate serum drug concentration or unknown obesity-related factors that make TNF-inhibitors less effective.

Our study contributes to the sparse literature evaluating dose escalation for HS patients with insufficient response to ADA40. In a European study, data from a previously-reported retrospective study of 14 White European patients treated with ADA80 for 12 weeks[4] were combined with retrospective data from 8 additional patients treated with ADA80 for 12 weeks and prospective data from 8 patients treated with adalimumab 80 mg every 12 days and 5 patients treated with adalimumab 80 mg every 10 days over a 24-week period, which demonstrated HiSCR-achievement in 66% of patients and median reduction of disease severity from severe to moderate.[5] Given that this study compares 3 different dosing intervals in one ethnic group, our findings generated from a racially diverse and more obese (median BMI 36.6 (32.5–40.7) vs 29.0 (25.3–33.4)) American cohort using a single dosing interval for a longer treatment period (13.2 (3.7–27.2) months vs 3–6 months) add meaningful clarity regarding the effectiveness of ADA80 for overweight and obese patients with moderate-to-severe HS.

Our study highlights the limitations of existing HS outcome measures. HS-PGA and HiSCR are responsive to disease change but are based on lesion counts which have been shown to have poor inter-rater reliability.[8] Moreover, HiSCR may have limited ability to capture treatment response in disease with extensive

tunneling and fibrosis. Although we assessed symptom improvement using subjective patient reports rather than validated surveys, pain is the single-most bothersome symptom associated with HS.[9] Thus improved pain, drainage, and quality of life may constitute markers of HS treatment response until improved measures are developed.

Despite sample size limitations and retrospective chart-review design, our findings support use of increased doses of adalimumab to achieve better disease control for overweight and obese HS patients and provide further justification for future randomized controlled trials examining weight-based dosing of adalimumab. Appropriately-dosed disease-modifying treatments prescribed early in disease course may have a role in preventing disease progression to irreversible scarring and disfigurement.[10,11] Thus, for patients with this debilitating disease, improvements in the availability and effectiveness of treatment regimens are critical for improving quality of life.

DISCLOSURES

Dr. Haley Naik has received grant support from AbbVie; consulting fees from 23andme, Abbvie, Aristea Therapeutics, Nimbus Therapeutics, Medscape, Sonoma Biotherapeutics, DAVA Oncology, Boehringer Ingelheim, Union Chimique Belge's (UCB) and Novartis; and investigator fees from Pfizer; and she holds shares in Radera, Inc. She is also an Associate Editor for JAMA Dermatology and a board member of the Hidradenitis Suppurativa Foundation.

Authors Williams, Guzik, and Wadhera have no disclosures to report.

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