

# Dapsone to Treat Moderate-to-Severe Hidradenitis Suppurativa: A Retrospective Case-Series

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## ABSTRACT

**Background:** Management of hidradenitis suppurativa (HS) is challenging since no single treatment provides consistently effective results, leaving patients with frequent relapses. Dapsone combines anti-microbial and anti-inflammatory properties that address aspects of HS pathogenesis. Few studies have evaluated the efficacy of oral dapsone on HS, especially in severe disease.

**Objective:** This study aims to evaluate the clinical outcomes of patients with moderate-to-severe HS treated with dapsone.

**Methods:** This retrospective chart review evaluated HS patients treated with oral dapsone over the past 10 years at one center. Treatment outcomes were classified based on Hurley staging, physician exam, and symptom progression. Adverse effects and concomitant treatment with dapsone were reviewed.

**Results:** Nineteen (19) patients with moderate-to-severe (Hurley Stage II-III) HS treated with oral dapsone were identified. Within 1-3 months, on dosages of dapsone varying from 25-100 mg/day, 3 patients (15.8%) had a clinically significant improvement in symptoms, 10 patients (52.6%) had a slight improvement, and 6 patients (31.6%) had no change in disease state; no patients deteriorated. The majority who improved were also on other medications, most commonly adalimumab. 4 patients experienced adverse effects, with nausea being most common; otherwise, dapsone was well-tolerated.

**Conclusions:** Dapsone may have some efficacy for moderate-to-severe HS and seems well-tolerated.

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## INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic, inflammatory skin disease characterized by recurrent nodules and abscesses that may rupture, leading to the formation of sinus tracts and scarring.<sup>1</sup> Lesions most frequently affect apocrine sweat gland-bearing areas within the intertriginous folds of the body. The initiating event is thought to be occlusion of the hair follicle secondary to follicular hyperkeratosis, leading to dilation and eventually rupture of pilosebaceous units.<sup>1</sup> Keratin and bacteria are subsequently released into the dermis leading to sustained chronic inflammation.<sup>2</sup> The sinus tract formation and scarring that occur as a result, are thought to be due to dysfunctional neutrophils releasing reactive oxygen species and proteases, causing tissue destruction.<sup>3</sup> Although the rationale for the follicular occlusion has yet to be defined, altered toll-like receptor (TLR) signaling due to a deficiency in the Notch signaling pathway on macrophages and dendritic cells may lead to increased production of pro-inflammatory cytokines. Interleukin (IL)-1 $\beta$ , IL-17, and particularly, tumor necrosis factor (TNF)- $\alpha$  play a major role in HS pathogenesis as overexpression has been linked to disease severity.<sup>4</sup>

Immunomodulatory, immunosuppressive, and antibiotic medications have been used to treat HS; however, response to these treatments is variable.<sup>5</sup> Topical clindamycin is most effective for superficial lesions and is indicated only for localized Hurley Stage I or mild Stage II disease.<sup>6</sup> The combined use of clindamycin (300 mg bid) and rifampicin (600 mg daily) for ten weeks is beneficial for widespread Hurley Stage I or mild Stage II disease, however, disease relapse has been reported in patients receiving this combination therapy after a one-year follow-up.<sup>6-8</sup> The combination of rifampicin (10 mg/kg daily), moxifloxacin (400 mg daily), and metronidazole (500 mg tid) for six weeks followed by rifampicin-moxifloxacin therapy is beneficial for Hurley Stage I or II disease or refractory disease.<sup>9</sup> Infliximab and adalimumab are TNF- $\alpha$  inhibitors with benefits for moderate to severe disease (Hurley Stages II-III) and improve quality of life.<sup>10</sup> Adalimumab was FDA-approved in 2015 for the treatment of HS. On the other hand, tetracyclines (500 mg bid.) and isotretinoin are systemic treatments that have little to no effect on HS.<sup>11,12</sup> Surgical intervention for persistent lesions may be considered alongside medical treatment.

Management of HS is challenging since no single treatment provides consistently effective results, leaving patients with frequent relapses. New treatment options are actively being explored as a result. Dapsone is a sulfonamide drug that is being considered as a possible agent for treating HS due to its antimicrobial and anti-inflammatory properties. Dapsone is bacteriostatic in action by competing with para-aminobenzoic acid for the active site of dihydropteroate synthetase, preventing bacterial folic acid synthesis.<sup>13</sup> Dapsone has several anti-inflammatory mechanisms of action. In addition to reducing pro-inflammatory cytokines, dapsone has specifically been shown to induce a dose-dependent suppression on TNF- $\alpha$ .<sup>14</sup> Dapsone suppresses the generation of reactive oxygen species and neutrophil elastase release through a dose-dependent reduction of intracellular and extracellular superoxide due to inhibition of calcium-dependent functions of neutrophils.<sup>15</sup> Since dapsone combines several qualities that address the pathogenesis of HS, it may be a promising treatment. With few studies, limited to case reports and two case-series, reporting the outcomes of dapsone treatment in HS, there is a need for more research into dapsone's effectiveness in HS. This study aims to evaluate the clinical outcomes of moderate-severe HS patients being treated with dapsone.

## MATERIALS AND METHODS

This retrospective chart review evaluated HS patients being treated with dapsone over the past 10 years at Wake Forest Baptist Medical Center Department of Dermatology. After receiving Institutional Review Board approval, the Wake Forest Baptist Medical Center Translational Data Warehouse database was queried to identify all patients with a diagnosis of HS (ICD-10: L73.2) and treatment with dapsone within the past ten years. Patients who were only prescribed the topical form or patients who were prescribed dapsone for a reason unrelated to HS were excluded from the analysis. Disease severity at dapsone initiation was determined using Hurley staging. This staging system classifies HS into three Stages: Stage I: abscess formation, single or multiple, without sinus tracts and cicatrization; Stage II: recurrent abscesses with tract formation and cicatrization, single or multiple, widely separated lesions; Stage III: diffuse or non-diffuse involvement, or multiple interconnected tracts and abscesses across the entire area.<sup>16</sup> Treatment outcome was determined by physicians' assessment of patients at scheduled follow-up visits and was classified as: "no change" if no improvement in the severity of symptoms was noted, "slight improvement" if minimal improvement was observed, "clinically significant improvement," if a large improvement was observed, and "deterioration" if clinical symptoms progressed during treatment.

## RESULTS

A total of 19 patients who have received dapsone treatment for HS were identified (Table 1). Of these patients, 13 were female and 6 were male (Table 2). The mean age of the included patients was 42.7 (range: 17-59). All patients had moderate to severe disease, with two patients having moderate (Hurley Stage II) disease and a total of 17 patients classified as severe (Hurley Stage III; Table 3). Several patients had disease refractory to other forms of treatment (Table 1). Glucose-6-phosphate dehydrogenase (G6PD) levels were normal for all patients.

All patients included in the study received dosages of dapsone varying from 25-100 mg/day (Table 1). Overall, a total of 3 patients had clinically significant improvement, 10 patients had slight improvement, 6 patients had no change in disease state, and zero patients had deterioration of disease status (Table 3). Of the three patients who showed clinically significant improvement, two of them received additional treatment with spironolactone 100 mg/day (patient 4) and doxycycline 200 mg/day (patient 15). Eight of the ten patients who had slight improvement and two of the six patients who had no change also received additional treatment. On average, the time to response was 2 months.

Treatment was well tolerated with the exception of four patients with nausea and fatigue being the most commonly reported adverse effects. The dose of dapsone for patient 1 was decreased from 150 mg/day to 100 mg/day after the patient experienced nausea at the higher dose. Treatment with rifampin (150 mg/day) was stopped for patient 3 after experiencing an ill-defined interaction with dapsone. Details about the specific reaction that took place was not documented in the medical records.

Eight patients received progressively increasing doses of dapsone. Increased dosing was beneficial for five of these patients, resulting in either clinically significant improvement or slight improvement.

A total of nine patients received additional treatment with adalimumab (Table 3). Of these nine patients, six experienced slight improvement during the combined treatment. No change was observed for the other three patients.

TABLE 1.

Summary of Clinical Presentations															
Patient	Age/ Gender	Race	Age at onset	Hurley Stage	Areas Af- fected	Smoking Status	BMI	Dapsone Dose (mg/day)	Outcome	Treatment Duration (months)	Time until reported im- prove- ment (months)	Side Effects	Additional Treat- ment	Topicals	Previously failed oral medications
1	37/F	Caucasian	25	III	Axilla, chest, thighs, groin	N	40.8	100-150	No change	19	2	Nausea, drop in Hgb	Adalimumab 40mg every other week	Silvadene, mupirocin, triamcinolone	Tetracycline, minocycline, doxycycline, trimethoprim/sulfamethoxazole, isotretinoin
2	59/M	Caucasian	29	III	Thighs, buttocks	N	32.9	25-50	No change	3	N/A	None	Clindamycin 300 mg/day, rifampin 300 mg/day	Chlorhexidene	--
3	36/F	Caucasian	16	III	Axillae, thighs	Y	39.8	50-100	Slight improvement	13	1	None	Spiro-nolactone 100 mg/day, Amoxicillin/clavulanate, glycopyrrolate 0.5 mg	Clindamycin	--
4	58/F	American Indian	48	III	Axillae, inframammary folds, pannus, inguinal folds	N	35.4	25-50	Slight improvement	8	3	Had interaction between with rifampin	Rifampin 150 mg/day, clindamycin 300 mg/day	--	--
5	33/M	Caucasian	N/A	III	Scalp, Axillae, groin	N	38.2	100	Slight improvement	6	N/A	None	Adalimumab 40 mg every other week, prednisone 25 mg/day	--	--
6	26/F	African American	14	III	Axillae, perium-bilical area, groin	N	35.4	100-150	Clinically significant improvement	28	2	None	Spiro-nolactone 100 mg/daily	--	Minocycline, spiro-nolactone, rifampin
7	50/M	African American	N/A	III	Scrotum	N	28.5	75	No change	3	N/A	None	--	Chlorhexidene, silvadene	Methotrexate, etanercept, adalimumab, tetracyclines, isotretinoin
8	58/F	African American	N/A	III	Buttocks, groin	Y	27.1	100	No change	6	N/A	None	Adalimumab 40mg every other week, Finasteride 5 mg	--	--
9	50/F	African American	N/A	II	--	Y	32.8	100	Slight improvement	3	1	None	--	Silvadene, clindamycin, benzoyl peroxide	-
10	42/F	African American	N/A	II	Inframammary folds, right posterior thigh, groin	N	41.3	75	Slight improvement	--	--	Stomach pain	Minocycline 200 mg/day	Clindamycin	--
11	57/F	Caucasian	N/A	III	Axillae, inframammary folds, groin	N	46.2	25-50	Clinically significant improvement	7	3	None	None	Clindamycin	Clindamycin, rifampin, spiro-nolactone, adalimumab, Kenalog injections
12	17/F	African American	8	III	Axillae, medial thighs, groin, mons pubis	Y	41.6	50-100	No change	13	N/A	None	None	--	--
13	50/M	Caucasian	N/A	III	Face, shoulders, back	Y	28.3	25-100	Slight improvement	13	2	None	Adalimumab 40 mg/week, isotretinoin 40 mg/day	Silvadene	--
14	51/F	N/A	26	III	Left axilla, left inguinal fold	N	31.1	50	Clinically significant improvement	N/A	N/A	None	Doxycycline 200 mg/day	--	Doxycycline, chlorhexidine wash
15	35/F	African American	29	III	Axillae, left breast, groin	Y	35.2	50	Slight improvement	11	1	None	Adalimumab 40 mg/week, spiro-nolactone 100 mg/day	--	--
16	41/F	Caucasian	N/A	III	Axillae, groin	Y	34.1	25	No change	3	N/A	Nausea, fatigue	Adalimumab 40 mg/week	Silvadene	Doxycycline, Kenalog injections
17	29/M	Caucasian	22	III	Axillae, upper thighs, groin, scrotum	Y	37.3	100	Slight improvement	9	1	None	Adalimumab 40 mg/week, Methotrexate 15 mg/week, doxycycline 200 mg/day, prednisone 20 mg/day, folic acid 1 mg/day	--	Methotrexate
18	42/M	African American	N/A	III	Neck, chest, buttocks	N	34.9	50	Slight improvement	4	1	None	Adalimumab 40 mg/week, moxifloxacin 400 mg/day, metro-nidazole 1000 mg/day, rifampin 300 mg/day	--	--
19	33/F	Caucasian	N/A	III	Axillae, groin, buttocks	N	44.1	100	Slight improvement	9	3	None	Adalimumab 40 mg/week, spiro-nolactone 200 mg/day, glycopyrrolate 4 mg/day	--	Metronidazole, rifampin, moxifloxacin

All patients had a normal G6PD status.

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TABLE 2.

Patient Demographics	
Characteristic (n=19)	Value (%)
Age (years)	
Mean	42.7
Range	17-59
Race	
Caucasian	9 (47.4%)
African-American	8 (42.1%)
American-Indian	1 (5.3%)
Gender	
Female	13 (68.4%)
Male	6 (31.6%)
Smoking Status	
Non-smoker	11 (57.9%)
Smoker	8 (42.1%)
Obesity	
Obese (BMI > 30)	16 (84.2%)
Overweight (BMI > 25)	3 (15.8%)
G6PD Normal	19 (100%)
Hurley Stage	
Stage I	0 (0%)
Stage II	2 (10.5%)
Stage III	17 (89.5%)
Other Conditions*	
Diabetes	2 (10.5%)
Crohn's disease	1 (5.26%)
Irritable bowel syndrome	1 (5.26%)
HIV	1 (5.26%)
History of prostate cancer	1 (5.26%)
History of ovarian and renal cancer	1 (5.26%)
Tinea versicolor	1 (5.26%)
Site of Disease*	
Groin	13 (68.4%)
Axillae	12 (63.2%)
Thighs	6 (31.6%)
Buttocks	3 (15.8%)
Chest	3 (15.8%)
Face/Scalp/Neck	3 (15.8%)
Inframammary folds	3 (15.8%)
Scrotum	2 (10.5%)
Back	1 (5.26%)
Previously Failed Systemic Medications*	
Doxycycline	4 (21.1%)
Rifampin	3 (15.8%)
Adalimumab	2 (10.5%)
Methotrexate	2 (10.5%)
Kenalog injections	2 (10.5%)
Minocycline	2 (10.5%)
Spironolactone	2 (10.5%)
Isotretinoin	2 (10.5%)
Etanercept	1 (5.3%)
Metronidazole	1 (5.3%)
Sulfamethoxazole/Trimethoprim	1 (5.3%)
Moxifloxacin	1 (5.3%)

\*Patients fall into more than one category

TABLE 3.

Treatment With Dapsone	
Characteristic (n=19)	Value (%)
Dose (mg)	
Mean	71.7
Median	50
Range	25-100
Treatment Duration (months)	
Mean	8.3
Range	3-28
Treatment Response	
Clinically significant improvement	3 (15.8%)
Slight improvement	10 (52.6%)
No change	6 (31.6%)
Deterioration	0 (0%)
Reported Side Effects*	
Nausea	2 (10.5%)
Fatigue	1 (5.3%)
Drop in Hemoglobin	1 (5.3%)
Stomach pain	1 (5.3%)
Reaction with rifampin	1 (5.3%)
Concomitant Medications*	
Topicals	9 (47.4%)
Silvadene	5 (26.3%)
Clindamycin	4 (21.1%)
Chlorhexidine	2 (10.5%)
Mupirocin	1 (5.3%)
Benzoyl Peroxide	1 (5.3%)
Triamcinolone	1 (5.3%)
Adalimumab	9 (47.4%)
40 mg per week	6 (31.8%)
40 mg every other week	3 (15.8%)
Spironolactone	4 (21.1%)
Rifampin	2 (10.5%)
Clindamycin	2 (10.5%)
Doxycycline	2 (10.5%)
Glycopyrrolate	2 (10.5%)
Amoxicillin/Clavulanate	1 (5.3%)
Isotretinoin	1 (5.3%)
Metronidazole	1 (5.3%)
Minocycline	1 (5.3%)
Moxifloxacin	1 (5.3%)
Prednisone	1 (5.3%)
Prednisone	1 (5.3%)

\*Patients fall into more than one category

**DISCUSSION**

Dapsone is a sulfone drug that possesses anti-microbial and anti-inflammatory properties and is used in a broad range of indications. In the case of severe disease with previously failed treatment attempts, TNF- $\alpha$  inhibitors (adalimumab, infliximab) may be an appropriate treatment option. Since these biologics and dapsone address the main pathophysiology of HS with their TNF- $\alpha$  TNF-inhibiting properties, the use of these two agents in conjunction may have a synergistic benefit. Few studies observing the effects of oral dapsone on HS have been published.<sup>17,18</sup> The most recent study was completed in 2011 and concluded that out of 24 patients, only 38% reported improvement. The patients who showed improvement had mild to moderate (Hurley Stage I-II) disease. A total of four patients in this study had severe (Hurley Stage III) HS and did not show any improvement. This study indicated that dapsone therapy is possible for patients with HS, particularly with milder cases.<sup>17</sup> Another retrospective study followed five patients with HS who received dapsone therapy with improvement being reported in all five patients within 4-12 weeks.<sup>18</sup> Overall, these previous studies support our results. However, our study differs from previous studies, with 89.5% of patients having severe (Hurley Stage III) disease.

In this retrospective review, 13/19 (68%) patients treated with dapsone showed improvement, while 6/19 (32%) did not have any change in symptoms (Table 3). Of the 13 patients who responded to treatment, 11 patients had advanced disease (Hurley Stage III; Table 1), suggesting the potential dapsone has as adjunctive therapy for moderate to severe disease (Hurley Stage II-III). The majority of the patients who showed improvement were also on combination therapy, either with immunomodulatory or antibiotic compounds. Of the two patients who were treated with monotherapy, one resulted in clinically significant improvement, and the other had no change.

This study has several limitations. The effectiveness of dapsone used as monotherapy cannot be determined as the majority of the patients were taking dapsone in combination with other agents. In addition, a quality-of-life survey to assess the overall satisfaction of patients before and after treatment was not performed. The possibility of disease recurrence while patients were either on dapsone or at the cessation of dapsone treatment also was not assessed. Finally, observations were based on a small patient population with no control group.

**CONCLUSIONS**

Dapsone may be an effective treatment option when used in combination with other therapies for moderate to severe (Hurley Stage II-III) HS. Further studies are required to clarify the effect of dapsone used as a monotherapy, to evaluate which treatment options work best in combination with dapsone, and to assess the possibility of disease recurrence in patients with moderate to severe disease who initially respond to dapsone therapy.

**DISCLOSURES**

Steven Feldman has received research, speaking, and/or consulting support from a variety of companies including Galderma, GSK/Stiefel, Almirall, Leo Pharma, Boehringer Ingelheim, Mylan, Celgene, Pfizer, Valeant, Abbvie, Samsung, Janssen, Lilly, Menlo, Merck, Novartis, Regeneron, Sanofi, Novan, Quriel, National Biological Corporation, Caremark, Advance Medical, Sun Pharma, Suncare Research, Informa, UpToDate and National Psoriasis Foundation. He is the founder and majority owner of www.DrScore.com and founder and part owner of Causa Research, a company dedicated to enhancing patients' adherence to treatment. Rita Pichardo has received consulting support from Abbvie. Brittany Baroudi and Arjun Bashyam have no conflicts to disclose.

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