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Interruption of oral clindamycin plus rifampicin therapy in patients with hidradenitis suppurativa: An observational study to assess prevalence and causes

To the Editor: Combination therapy with oral clindamycin, 300 mg twice daily, plus rifampicin, 300 mg twice daily or 600 mg once daily, for 10 weeks is among the keystone treatments for moderate-to-severe hidradenitis suppurativa (HS).[1] Since 2006, 6 small studies involving a total of 178 patients have investigated the efficacy of this antibiotic combination.[2-4] Most of the studies had a retrospective design, and only 1 reported safety outcomes.[4] The prevalence of treatment interruption ranged from 9.1% to 28.6% (mean, 16.3%), and the rate of appearance of adverse events ranged from 9.1% to 38.3% (mean, 21.9%).[2-4] The most common adverse events were gastrointestinal (GI) disturbances (diarrhea, vomiting, abdominal pain, and dyspepsia), followed by cutaneous rash, vaginitis, nonspecific pain, and arthralgia.

A better understanding of the reasons for poor adherence and adverse events associated with treatment may help dermatologists to better advise patients, potentially allowing prevention of some side effects.

We designed a descriptive, observational, retrospective multicentric study to determine the prevalence of interruption of clindamycin plus rifampicin before 10 weeks in patients with HS. A retrospective chart review was performed; included were patients who were at least 18 years old, had Hurley stage II or III HS, and were receiving clindamycin plus rifampicin for the first time. Patients simultaneously receiving other systemic therapies for HS were excluded.

We enrolled 509 patients from 14 Spanish hospitals (Table I); 135 of them (26.5%) interrupted antibiotic treatment. We did not observe differences between the proportions of men (26.6%) and women (26.5%) who interrupted their treatment. After dividing the study population into quartiles by age (≤30 years, n = 133; 31-38 years, n = 127; 39-49 years, n = 125; and ≥50 years, n = 124), we observed that older age was associated with interruption of treatment. The odds ratio (OR) for treatment interruption in patients aged 50 or older versus patients in the youngest age group was 1.9 (95% confidence interval [CI], 1.1-3.3; $P = .03$). Ever-smokers had 1.5 times the odds of interrupting their treatment as compared with never-smokers (95% CI, 1.1-2.1; $P = .02$). In multivariable

Table I. Demographic characteristics of enrolled patients according to Hurley stage of HS, with treatment interruption and adverse events rates

Characteristic	Total	Hurley stage		*P* value
		II*	III†	
All patients, n (%)	509	378 (74.2)	131 (25.8)	
Female, n (%)	272 (53.4)	215 (57)	57 (43.5)	.008
Male, n (%)	237 (46.6)	163 (43)	74 (56.5)	
Median age, y (IQR)	38 (30-49)	36 (28-47)	45 (36-54)	<.001
BMI (kg/m^2), n (%)				
<25	133 (26.1)	92 (24.3)	41 (31.3)	.17
≥25	344 (67.6)	259 (68.5)	85 (64.9)	
Unknown	32 (6.3)	27 (7.1)	5 (3.8)	
Ever-smoker, n (%)	360 (70.7)	268 (70.9)	92 (70.2)	.88
Median age at onset of HS, y (IQR)	20 (16-29)	20 (16-29)	20 (16-30)	.93
Median duration of HS, y (IQR)	14 (5-24)	12 (4-20.5)	20 (8.8-29.3)	<.001
Median No. of affected locations (IQR)	3 (2-4)	3 (2-4)	3 (2-6)	<.001
Lesion location, n (%)				
Axillae	326 (64.0)	231 (61.1)	95 (72.5)	.019
Groin	334 (65.6)	237 (62.7)	97 (74.0)	.018
Breasts	109 (21.4)	75 (19.8)	34 (26.0)	.142
Gluteus	186 (36.5)	114 (30.2)	72 (55.0)	<.001
Abdomen	101 (19.8)	68 (18.0)	33 (25.2)	.075
Genitals	167 (32.8)	93 (24.6)	74 (56.5)	<.001
Treatment interrupted, n (%)	135 (26.5)	106 (28.0)	29 (22.1)	.19
Adverse events, n (%)	145 (28.5)	116 (30.7)	29 (22.1)	.062

BMI, Body mass index; *HS*, hidradenitis suppurativa; *IQR*, interquartile range.
*Hurley stage II: recurring boils in multiple areas with scarring and sinus tracts.
†Hurley stage III: widespread boils with multiple interconnected tracts across the affected area, with no normal-appearing skin left between them.

Table II. Demographic and disease characteristics related to treatment interruption

Variable	Treatment interrupted, % (n/N)	OR (95% CI)	*P* value	OR_a (95% CI)	*P* $value_a$
Female	73.4% (174/237)	1.0 (0.7-1.5)	.98	—	—
Male	26.6% (63/237)				
Age, y					
≤30	20.3% (27/133)	1	—	1	—
31-38	26.8% (34/127)	1.4 (0.8-2.5)	.22	1.4 (0.8-2.5)	.26
39-49	27.2% (34/125)	1.5 (0.8-2.6)	.19	1.4 (0.8-2.5)	.27
≥50	32.3% (40/124)	1.9 (1.1-3.3)	.030	1.8 (1.0-3.1)	.048
BMI ≥25 kg/m^2	28.2% (97/344)	1.4 (0.9-2.2)	.21	—	—
Smoking	29.4% (106/360)	1.5 (1.1-2.1)	.02	1.7 (1.0-2.7)	.033
Age at onset, y					
≤16	25% (33/132)	1	—	—	—
17-20	28.1% (39/139)	1.2 (0.7-2.0)	.57	—	—
21-29	24.5% (27/110)	1.0 (0.5-1.8)	.94	—	—
≥30	27.9% (34/122)	1.2 (0.7-2.0)	.60	—	—
Mean duration of HS ≤5 y	23.4% (32/137)	0.8 (0.5-1.3)	.34	—	—
Hurley stage II	28% (106/378)	1.4 (0.9-2.2)	.19	—	—
≤2 affected locations	29.6% (67/226)	1.3 (0.9-2.0)	.15	—	—

BMI, Body mass index; *CI*, confidence interval; *OR*, odds ratio; OR_a, adjusted odds ratio; *P* $value_a$, adjusted *P* value.

analysis, these associations remained significant (for smoking: OR, 1.7; 95% CI, 1.0-2.7; $P = .033$; for age ≥50: OR, 1.8; 95% CI, 1.0-2.7; $P = .048$). We did not observe any association between treatment interruption and any other feature (Table II). There were 182 adverse effects in

145 patients (28.5%), the most frequent being GI disturbances (n = 108 [21.2%]), followed by nonspecific aches or pains (n = 19 [3.7%]) and mucocutaneous *Candida albicans* infections (n = 12 [2.4%]). None of the patients with GI disturbances presented with *Clostridium difficile* colitis, and all responded well to conservative management. No association between adverse events and any of the demographic or disease characteristics considered was observed.

In conclusion, to our knowledge, this is the largest reported series of patients treated with a combination of clindamycin plus rifampicin for HS. We observed higher rates of treatment interruption and prevalence of adverse effects than previously reported. Patients aged 50 years or older and smokers were more prone to interrupt their treatment. GI disturbances were the most frequent adverse effects in our population. Physicians may consider prescribing probiotics to these patients at higher risk of GI side effects.[5]

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