

# The Effect of Combined Treatment with Oral Clindamycin and Oral Rifampicin in Patients with Hidradenitis Suppurativa

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## Key Words

Acne inversa · Antibiotics therapy · Clindamycin · Rifampicin

## Abstract

**Background:** A previous limited study showed promising results of combined oral treatment with rifampicin 600 mg and clindamycin 600 mg for 10 weeks. **Objective:** To expand and to validate the basis for this therapy, we reviewed the response to different treatment durations. **Method:** A retrospective study in 34 patients. **Results:** Twenty-eight of 34 patients (82%) experienced at least partial improvement, and 16 (47%) showed a total remission. The maximum effect of treatment appeared within 10 weeks. Following total remission, 8 of 13 (61.5%) patients treated as mentioned above experienced a relapse after a mean period of 5.0 months. Nonresponders were predominantly patients with severe disease. **Conclusion:** Combination treatment with oral rifampicin and clindamycin is a promising treatment option for hidradenitis suppurativa, despite the frequent occurrence of diarrhea as a side effect. The length and the dosage of treatment are not yet firmly established.

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## Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease characterized by recurring painful abscesses and draining sinuses in the anogenital-inguinal area and axillae, with a prevalence of 1% [1]. It has a significant impact on the patients' quality of life [2, 3]. The exact cause of HS remains unclear [4]. Histopathological studies have suggested occlusion of the follicular infundibulum as an important factor [5, 6]. A large variety of microorganisms can be isolated from the lesions, but often lesions appear to be sterile [7, 8]. *Staphylococcus epidermidis* species are the most frequently cultured bacteria, and *Staphylococcus aureus* is found in a minority of lesions [7, 8]. Other data however suggest that HS patients may suffer from low-grade bacteremia, indicating that bacteria may play a role [9]. HS is currently thought of as being a sterile inflammation, but bacteria are suspected of playing a role in the disease process, although not that of a simple infection. It is speculated that bacteria may play a part through immune-mediated mechanisms of inflammation in association with a dysregulated immune response in the hair follicles [4]. Antibiotic therapy is however widely used and mentioned in all textbooks of

**Table 1.** Patient characteristics

Number	34
Sex (F/M)	29/5
Age, years	
Mean	39.9
Range	19–59
Duration of HS, years	
Mean	17.8
Range	1–52
Disease severity	
Hurley 1	4 (11.8)
Hurley 2	20 (58.8)
Hurley 3	10 (29.4)
Affected areas	
Groin	26 (77.5)
Axillae	12 (35.3)
Genitalia	8 (23.5)
Buttocks	8 (23.5)
Perianal	4 (11.8)
Other	2 (5.9)
Previous medication	
Oral antibiotics	23 (67.6)
Surgery	22 (64.7)
Isotretinoin	12 (35.3)
Resorcinol	10 (29.4)
Topical antibiotics	9 (26.5)
Acitretin	3 (8.8)
Infliximab	1 (2.9)
Prednisone	1 (2.9)

Figures in parentheses are percentages.

dermatology as a prominent form of treatment for HS. Curiously the literature reveals only a handful of studies on the use of antibiotics. Topical clindamycin was found to be superior to placebo in a randomized double-blind clinical trial, and in another randomized clinical trial there was no difference between systemic tetracycline 1 g daily and topical clindamycin 1% twice daily [10, 11]. A case report of 2 patients using systemic clindamycin in a high dose of 1,200 and 2,400 mg, respectively, showed good improvement albeit with relapse on cessation of treatment [12]. The combination therapy with oral clindamycin and oral rifampicin has been suggested to be an effective treatment for other follicular occlusion disorders such as folliculitis decalvans [13, 14]. Combined treatment with oral rifampicin 300 mg b.i.d. and oral clindamycin 300 mg b.i.d. for 10 weeks has been advocated for HS [15, 16]. In order to assess the validity of these claims, a review was made of the outcomes of combined oral clindamycin and oral rifampicin treatment of consecutive patients in two dermatology centers.

## Subjects and Methods

In total, 47 patients with a diagnosis of HS were treated with the therapy of combined oral clindamycin and oral rifampicin at the dermatology departments of the Deventer Hospital, the Netherlands, and Roskilde Hospital, Denmark, between 2006 and 2007. Information about age, sex, duration of HS, sites of inflammation, previous treatment, the outcome of clindamycin and rifampicin treatment, side effects and follow-up were extracted from the records. All included patients had had active disease for many months or years and had failed several other HS treatments including topical clindamycin, other oral antibiotics and surgery prior to the clindamycin and rifampicin combination treatment (table 1). The combination treatment used in this study was not the first choice of disease management. The decision to use this treatment was taken by J.B. (Deventer) or G.J. (Roskilde). Thirteen patients were excluded because of concomitant oral or topical medication. Descriptive staging of disease severity based on the assessment of scarring and inflammation according to Hurley [17] was made: stage 1 = abscess formation, single or multiple without sinus tracts and cicatrization; stage 2 = recurrent abscesses with tract formation and cicatrization, single or multiple widely separated lesions; stage 3 = diffuse or nearly diffuse involvement or multiple interconnected tracts or abscesses across the entire area. Patient characteristics are given in table 1. Outcomes were presented as a physician global assessment and were classified according to the effect of the treatment on inflammation including suppuration, whereas the presence of noninflamed lesions such as sinus tracts or scars was not considered. Partial improvement was defined as less than 75% clinical improvement from baseline, whereas total remission was defined as total clearance or at least improvement by more than 75%.

## Results

Five different dosage regimens were used. Four dosage regimens contained only 7 or fewer patients. Outcomes are presented according to the intention-to-treat principle. In the group as a total, 28 of 34 patients (82.4%) responded to treatment, 12 (35.3%) showed partial improvement and 16 (47.1%) total remission. Six (17.6%) patients showed no improvement (table 2). No cases of worsening of the disease were observed during the treatment period. There was not much difference in outcomes between patients treated for 10 weeks or longer compared to patients who were treated for shorter than 10 weeks. Outcomes according to the Hurley classification at onset are shown in table 3. Patients with no response were predominantly patients with severe disease. Adverse side effects occurred in 13 of 34 patients (38.2%), of which diarrhea was the most common, in 9 patients (26%). In addition, 2 patients experienced a *Candida* vaginitis, 2 nausea, 2 dizziness and 1 glossodynia. Nine patients (26%) stopped treatment due to the side effects. Six of these 9

**Table 2.** Outcomes according to different treatment durations

	Any dosage of clindamycin + rifampicin combination			Clindamycin 2 × 300 mg, rifampicin 2 × 300 mg		
	<10 weeks (n = 13)	≥10 weeks (n = 21)	any weeks (n = 34)	<10 weeks (n = 7)	≥10 weeks (n = 16)	any weeks (n = 23)
No improvement	1 (7.7)	5 (23.8)	6 (17.6)	0	3 (16.8)	3 (13)
Partial improvement	6 (46.2)	6 (28.6)	12 (35.3)	3 (42.9)	4 (25)	7 (30.4)
Total remission	6 (46.2)	10 (47.6)	16 (47.1)	4 (57.1)	9 (56)	13 (56.5)

Figures in parentheses are percentages.

**Table 3.** Outcomes according to Hurley score at onset

	Any dosage of clindamycin + rifampicin combination			Clindamycin 2 × 300 mg, rifampicin 2 × 300 mg		
	Hurley 1 (n = 4)	Hurley 2 (n = 20)	Hurley 3 (n = 10)	Hurley 1 (n = 1)	Hurley 2 (n = 15)	Hurley 3 (n = 7)
No improvement	1 (25)	1 (5)	4 (40)	0	0	3 (43)
Partial improvement	1 (25)	9 (45)	2 (20)	0	6 (40)	1 (14)
Total remission	2 (50)	10 (50)	4 (40)	1 (100)	9 (60)	2 (29)

Figures in parentheses are percentages.

patients discontinued due to diarrhea. The largest subgroup of patients studied was treated according to the scheme of Mendonça and Griffiths [15] (n = 23). This group was therefore further analyzed. Thirteen (56.5%) patients experienced total remission, 7 (30.4%) partial improvement and 3 (13%) no improvement. All nonresponders in this group were Hurley stage 3. Following total remission in this group, 8 of 13 patients (61.5%) experienced a relapse of the disease after a mean of 5.0 months (range 0.3–18 months). Three patients (23.1%) were still in remission at the end of study after a mean follow-up of 7.3 months (range 1–12 months). Two (15.4%) patients with total remission were lost to follow-up.

## Discussion

This study shows that treatment of HS with combined oral clindamycin and oral rifampicin results in clinical improvement in 28 of 34 patients (82.4%). Our results are in agreement with those of Mendonça and Griffiths [15] as well as Gener et al. [16]. Mendonça and Griffiths [15] showed that the combined treatment with oral clindamycin 300 mg b.i.d. and oral rifampicin 300 mg b.i.d. for 10

weeks was effective in 10 of 14 (71.4%) treated patients. Gener et al. [16] showed in a large series of 116 consecutive patients complete remission in 8 of the finally analyzed 70 patients (11%), improvement in 60 of 70 patients and worsening in 2 of 70 patients after 10 weeks of the combined treatment. Our study has some limitations because it was a retrospective study and further there was heterogeneity in the group of HS patients included; it does however reflect clinical practice and variation. Although a 10-week treatment period seems rather short for a chronic fluctuating disease like HS, we did not observe large differences in outcomes between patients treated for 10 weeks and longer and patients treated for a shorter period. Actually, a higher percentage of nonresponders were observed in the group treated for 10 weeks or longer, indicating that shorter treatment duration may be effective. Furthermore the response to treatment tends to correlate with the disease severity as all nonresponders in the 10-week course [15] had stage 3, i.e. those with significant scarring of a larger affected area. However, not many Hurley 1 patients were treated making a more precise estimate of the influence of disease severity on outcome more difficult. Most patients who achieved total remission at the end of treatment in the 10-week course [15]

also experienced a relapse after a mean of 5.0 months (range 0.3–18 months). This may indicate that the used antibiotics do not cure the disease but relieve the symptoms. A 5-month disease-free period does not look long, but for these chronic HS patients it was quite a relief. The number of patients experiencing side effects in this study was quite high, 13 of 34 patients (38.2%) making 9 of 34 patients (26%) to discontinue this regimen. This side effect rate was higher than that of Gener et al. [16], who showed that 10 of 70 patients (14%) experienced side effects, making 8 of 70 (11%) to discontinue this regimen. This high incidence of side effects forms the major drawback of this combination treatment schedule and hampers the usefulness in daily practice. Clindamycin usage is associated with the development of *Clostridium difficile* colitis. None of the patients with diarrhea in this study experienced a *C. difficile* colitis. The mechanism of action of these two drugs in HS needs further elucidation. A significant proportion of HS lesions appear to be sterile [7, 8], and anti-inflammatory therapy with e.g. cyclosporine [18], dapsone [19], methotrexate [20], prednisone [21] or biologicals [22] has been described as an alternative therapy to antibiotics in HS. Moreover, besides their bactericidal effects the antibiotics used in the treatment of HS also have immunomodulatory properties [23], suggesting that the latter property is also responsible for their beneficial effect in HS. Rifampicin is a derivative of *Streptomyces mediterranei*. It is a lipid-soluble, broad-spectrum antibacterial agent which acts by binding to and inactivating bacterial deoxyribonucleic-acid-dependent ribonucleic acid polymerase [24]. It can sterilize staphylococcal abscesses [25] and maintains its bacterio-

lytic effect even when the targets are engulfed in phagocytic cells [26]. It inhibits the growth of the majority of Gram-positive bacteria as well as many Gram-negative microorganisms [27]. Rifampicin is highly active against both *S. aureus* and coagulase-negative staphylococci. Furthermore, bacterial resistance can occur rapidly when rifampicin is used as monotherapy. In addition to its antimicrobial effects, it also modifies cell-mediated hypersensitivity, by suppressing antigen-induced transformation of sensitized lymphocytes, and T-cell function [23]. Clindamycin is the chlorine-substituted successor to lincocmycin. It binds to the 50S subunit of the bacterial ribosome and inhibits the early stages of protein synthesis. The antimicrobial effect is primarily bacteriostatic. It is active against Gram-positive cocci except enterococci and most anaerobic bacteria [28]. Like rifampicin, clindamycin has the potential to modify or suppress inflammation. It suppresses the complement-derived chemotaxis of polymorphonuclear leukocytes in vitro, reducing inflammation [29]. In addition, rifampicin and clindamycin have effective bactericidal action when given together [30]. HS is a notoriously difficult-to-treat disease, and the encouraging results of this retrospective case series and that of Gener et al. [16] emphasize the need for a large prospective, dose-finding, randomized controlled clinical trial.

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