Clindamycin Mono-Therapy of Hidradenitis Suppurativa Patients: A Single-Center Retrospective Study

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Background: A rifampicin (RF)-clindamycin (CL) combination therapy is recommended as the first-line treatment for moderate to severe hidradenitis suppurativa (HS). Although the long-term use of RF requires caution due to the possibility of developing resistant bacteria, only a few studies have investigated alternatives for this combination therapy.

Objective: To evaluate the efficacy of systemic CL mono-therapy and assess the prevalence and CL resistance of bacterial growth in HS patients.

Methods: A total of 53 HS patients treated with CL mono-therapy were included. The efficacy was evaluated by identifying the rate of HS Clinical Response (Hi-SCR) achievers and comparing HS Physician’s Global Assessment (HS-PGA) before (W0) and after (W8) the treatment. Purulent material from HS skin lesions was collected on the W0. Bacterial flora and antibiotic sensitivity were determined by bacterial cultures.

Results: Of 53 HS patients, 34 were eligible for evaluation of the efficacy of the therapy. Twenty-one patients (61.76%) achieved Hi-SCR. The mean scoring of HS-PGA had significantly decreased from 3.24 to 2.15 (p=0.001). The prevalence of CL resistance was 15.00%. No significant differences in the efficacy of the therapy according to the presence of CL-resistant bacteria on the W0 were observed (p=0.906). Adverse events occurred in 26.42% of patients.

Conclusion: Systemic CL mono-therapy may be a safe and useful alternative to RF-CL combination therapy, and no significant difference in the efficacy of the therapy depending on the presence of CL-resistant bacteria was observed.

Keywords: Anti-bacterial agents resistance, Clindamycin mono-therapy, Hidradenitis suppurativa

INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic, recurrent, debilitating, inflammatory, skin follicular disease that usually presents with painful, deep-seated, inflamed lesions after puberty. These lesions are found in the apocrine gland-bearing areas of the body, most commonly, in the axillae, inguinal, and anogenital region. The etiology of HS is multifactorial and remains unclear. Dysregulation of the pilosebaceous unit and an altered immune response have been recognized as crucial pathogenic factors for the onset of HS. Though HS is not primarily an infectious disease, bacterial specimens can often be isolated from exudates of the HS lesion and the role of bacteria in the early phase of the disease is known as an important trigger of the inflammatory response. Indeed, studies exploring the bacteriology of HS lesions have found the involvement of various bacterial species, with frequent culture isolation or genomic identification of a polymicrobial microflora dominated by coagulase-negative staphylococcal species and mixed anaerobic bacteria, with Staphylococcus aureus and streptococcal species also isolated from a substantial proportion of lesions. For this reason, antibiotic therapy is one of the first steps in the management of HS, and the rifampicin (RF)-clindamycin (CL) combination is recommended as first-line therapy in moderate...
to severe HS for their anti-microbial, anti-inflammatory, and immune-modulatory properties. However, the long-term use of RF may induce several adverse events and the possibility of developing resistant bacteria. Also, RF is a potent inducer of cytochrome P450 3A4 and was shown to decrease CL serum levels to a significant extent.

However, only limited studies are investigating possible alternatives to this therapy and the prevalence of antibiotics resistance on several HS bacterial isolates. Thus, this study aimed to retrospectively evaluate the efficacy of systemic CL monotherapy and assess the prevalence and CL resistance of bacterial growth in HS patients.

MATERIALS AND METHODS

Patient selection
In the period between January 1, 2015 and January 31, 2020, HS patients who were treated with CL mono-therapy at CHA Bundang Medical Center were studied retrospectively. CL-mono therapy was conducted to reduce the occurrence of resistant bacteria and to increase patient compliance by reducing side effects caused by RL usage. From this group, bacterial antibiotic resistance profiles and microbiological reports of the patients who had undergone bacterial culture tests before starting CL mono-therapy were also studied. Patients who were lost to follow-up or had inadequate medical information in the patient electronic chart were excluded from the analysis. The following data were collected: sex, age, body mass index (BMI), localization of the HS lesions, disease duration as recalled by the patient, smoking history, comorbidities, previous treatment modalities, Hurley’s stage, Hidradenitis Suppurativa Clinical Response (Hi-SCR) measure, Hidradenitis Suppurativa Physician’s Global Assessment (HS-PGA) measure, and adverse events of CL mono-therapy. Ethical approval was obtained from the ethics committee of CHA Bundang Medical Center (IRB no. 2019-07-066).

Assessment
Efficacy of the treatment was evaluated by identifying the rate of Hi-SCR (as at least a 50% reduction from baseline in the total abscess and inflammatory nodule count, with no increase in the abscess or draining tunnel count) achievers and comparing HS-PGA before (W0) and after (W8) the treatment. Purulent materials from the HS patients were collected on the W0. Bacterial flora and antibiotics sensitivity were determined by bacterial cultures.

Statistical analysis
The distributions of patient characteristics were described using standard deviation. The measures on W0 and W8 were compared using the Wilcoxon matched-pairs signed-rank test. Associations between the efficacy of the treatment and CL resistance were evaluated using the chi-square test. Statistical significance was considered when the p-value was below 0.05. Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Study participants
A total of 53 HS patients treated with CL mono-therapy were included in this study, consisting of 34 males and 19 females (sex ratio 1.79). Their mean age was 28.64±9.82 years. The mean BMI was 26.66±5.27 kg/m². Furthermore, 34 patients (64.15%) were on Hurley’s stage III, 15 patients (28.30%) were on Hurley’s stage II, and 4 patients (7.65%) were on Hurley’s stage I. Demographics and clinical characteristics of the patients are shown in Table 1.

Clinical response
Of the 53 patients, 34 were eligible for evaluation of the efficacy of the treatment on the W8. Among them, 21 patients (61.76%) achieved Hi-SCR. According to Hurley’s stage classification, 100% of Hurley’s stage I patients, 80.00% of Hurley’s stage II patients, and 52.17% of Hurley’s stage III patients achieved Hi-SCR. The mean scoring of HS-PGA had significantly decreased from 3.24 to 2.15 from the W0 to the W8 (p=0.001). When classified according to severity, the mean scoring of HS-PGA for the clear-moderate group had significantly decreased from 2.68 to 1.56 from the W0 to the W8 (p=0.002). Whereas, the mean scoring of HS-PGA for the severe-very severe group had decreased from 4.78 to 4.12 from the W0 to the W8 (p=0.083; Table 2).

Prevalence and Clindamycin resistance of bacterial isolates
In 30 lesions, purulent materials were collected on the W0. Of these, 34 bacterial culture growths were included in the analy-
Of the 34 positive bacterial cultures, 27 isolates (79.41%) were Gram-positive, while 7 (20.59%) were Gram-negative. Among them, anaerobic bacteria were observed in 1 case (2.94%). The most frequent bacterial families identified included Staphylococcaceae (61.76%), Enterobacteriaceae (14.71%), and Streptococcaceae (5.88%). The most frequent genus or species identified were Staphylococcus epidermidis (32.35%), S. aureus (8.82%), and Escherichia coli (8.82%), as outlined in Table 3. Antibiotics with a high rate of resistance were Penicillin (94.74%), Erythromycin (21.05%), and Ciprofloxacin (17.39%). The prevalence of CL resistance was 15.00%. There was no statistically significant difference in the efficacy of CL monotherapy according to the presence of CL-resistant bacteria on the W0 (p=0.906). Antibiotics such as Vancomycin, Linezolid, and Teicoplanin showed the highest antibiotics sensitivity with 100.00% sensitivity. Sensitivity test profiles are summarized in Table 4.

Of the patients who had a bacterial culture test on the W0, 8 patients had a follow-up bacterial culture tests on the W8. Of these, 10 bacterial culture growths were included in the analysis. Of the 10 positive bacterial cultures, 6 isolates (60.00%) were Gram-positive, while 4 (40.00%) were Gram-negative. There were no anaerobic bacteria observed. The most frequent bacterial families identified included Staphylococcaceae (61.76%), Enterobacteriaceae (14.71%), and Streptococcaceae (5.88%). The most frequent genus or species were Staphylococcus epidermidis (20.00%), E. coli (20.00%), and Dermabacter hominis.
(20.00%) (Table 3). Antibiotics with a 100% resistance were Ampicillin, Ampicillin/Sulbactam, Ciprofloxacin, Minocycline, CL, Erythromycin, Methicillin, Oxacillin, and Penicillin. Antibiotics such as Vancomycin, Linezolid, and Teicoplanin showed the highest antibiotics sensitivity with 100.00% sensitivity (Table 4).

### Safety

Of the 53 patients, 14 patients (26.42%) experienced an adverse event and 9 patients (16.98%) discontinued treatment due to these treatment-related adverse events. The most common adverse event was diarrhea, which was observed in 12 cases. After further gastroenterological evaluation, none of the patients with diarrhea were diagnosed with pseudomembranous colitis. Other adverse events were abdominal pain (1 case), skin rash (1 case), the elevation of liver enzyme levels (1 case), and weight gain (1 case). All adverse events ceased after discontinuation of the treatment.

### DISCUSSION

Though HS is not primarily an infectious disease, the RF-CL combination is recommended as first-line therapy in moderate to severe HS for their anti-microbial, anti-inflammatory, and immune-modulatory properties. However, there are still several concerns regarding long-term RF-CL combination treatment.

RF resistance is an important issue in treating tuberculosis, especially in tuberculosis endemic regions. To counter the threat of resistance, RF should be preserved, as its use in combination therapy for non-mycobacterial infections is ever more frequent. From the pharmacokinetic perspective, previous studies have demonstrated that co-treatment with RF reduces CL plasma concentrations. This phenomenon can be correlated with the ability of RF to induce the cytochrome P450 3A4, which is responsible for CL metabolism. Next, a possible effect of RF on the intestinal microbiota is present. Indeed, Namasivayam et al. have studied the impact of tuberculosis anti-

### Table 3. Bacterial isolates from purulent material drained from Hidradenitis suppurativa lesions at baseline and week 8

| Family          | Genus or species                          | Number of bacteria isolates | Gram positive/negative | Aerobic/Anaerobic       |
|-----------------|-------------------------------------------|----------------------------|------------------------|-------------------------|
|                 |                                           | Baseline Week 8             |                        |                         |
| **Staphylococcaceae** |                                           |                           |                        |                         |
|                 | *Staphylococcus aureus*                   | 3                         | -                      | Positive Facultative anaerobic |
|                 | *Staphylococcus epidermidis*              | 11                        | 2                      | Positive Facultative anaerobic |
|                 | *Staphylococcus haemolyticus*             | 1                         | -                      | Positive Facultative anaerobic |
|                 | *Staphylococcus caprae*                   | 1                         | -                      | Positive Facultative anaerobic |
|                 | *Coagulase-negative Staphylococcus*       | 2                         | -                      | Positive Facultative anaerobic |
|                 | *Staphylococcus lugdunensis*              | 2                         | -                      | Positive Facultative anaerobic |
|                 | *Staphylococcus warneri*                  | 1                         | -                      | Positive Facultative anaerobic |
| **Streptococcaceae** |                                           |                           |                        |                         |
|                 | *GAS (B-hemolytic streptococcus; group A)* | 1                         | -                      | Positive Facultative anaerobic |
|                 | *GBS (B-hemolytic streptococcus; group B)* | 1                         | -                      | Positive Facultative anaerobic |
| **Enterococcaceae** |                                           |                           |                        |                         |
|                 | *Enterococcus faecalis*                   | 1                         | 1                      | Positive Facultative anaerobic |
| **Enterobacteriaceae** |                                         |                           |                        |                         |
|                 | *Escherichia coli*                        | 3                         | 2                      | Negative Facultative anaerobic |
|                 | *Enterobacter aerogenes*                  | 1                         | 1                      | Negative Facultative anaerobic |
|                 | *Klebsiella pneumoniae*                   | 1                         | -                      | Negative Facultative anaerobic |
| **Pseudomonaceae** |                                           |                           |                        |                         |
|                 | *Pseudomonas aeruginosa*                  | 1                         | 1                      | Negative Aerobic         |
| **Corynebacteriaceae** |                                         |                           |                        |                         |
|                 | *Corynebacterium species*                 | 1                         | -                      | Positive Aerobic         |
| **Lactobacillaceae** |                                           |                           |                        |                         |
|                 | *Pediococcus pentosaceus*                 | 1                         | -                      | Positive Facultative anaerobic |
| **Propionibacteriaceae** |                                         |                           |                        |                         |
|                 | *Propionibacterium acnes*                 | 1                         | -                      | Positive Anaerobic       |
| **Morganellaceae** |                                           |                           |                        |                         |
|                 | *Proteus mirabilis*                       | 1                         | -                      | Negative Facultative anaerobic |
| **Dermabacteriaceae** |                                         |                           |                        |                         |
|                 | *Dermabacter hominis*                     | -                         | 2                      | Positive Facultative anaerobic |
| **Actinomycetaceae** |                                           |                           |                        |                         |
|                 | *Actinomyces europaeus*                   | -                         | 1                      | Positive Facultative anaerobic |
microbial treatment on the diversity and composition of the intestinal microbiota in infected mice, demonstrating the main role played by RF on anti-tuberculosis induced dysbiosis.

We have studied the efficacy of 8 weeks of systemic CL mono-therapy in reducing the risk of side effects and the emergence of resistant bacteria related to RF and assessed the prevalence and CL resistance of bacterial growth in HS patients.

After 8 weeks of treatment with CL mono-therapy, we observed an improvement in the disease activity as assessed by Hi-SCR and HS-PGA. Comparing these results according to severity, the efficacy of CL mono-therapy was higher in mild to moderate than severe to very severe cases. The results of our

| Antibiotic                        | Baseline |        | Week 8  |        |
|-----------------------------------|----------|--------|---------|--------|
|                                   | Resistance | Sensitivity | Resistance | Sensitivity |
| Amikacin                          | 0 (0)    | 6 (100) | 0 (0)   | 2 (100) |
| Amoxicillin/Clavulanic acid       | 1 (20.00) | 4 (80.00) | 1 (50.00) | 1 (50.00) |
| Ampicillin                        | 2 (40.00) | 3 (60.00) | 2 (100)  | 0 (0)   |
| Ampicillin/Sulbactam              | 1 (100)  | 0 (0)   | 1 (100)  | 0 (0)   |
| Aztreonam                         | 0 (0)    | 6 (100) | 0 (0)   | 2 (100) |
| Ceftazidime                       | 0 (0)    | 6 (100) | 0 (0)   | 2 (100) |
| Ciprofloxacin                     | 4 (17.39)| 19 (82.61)| 3 (100)  | 0 (0)   |
| Colistin                          | 0 (0)    | 1 (100) | 0 (0)   | 1 (100) |
| Cefazolin                         | 1 (20.00)| 4 (80.00)| 1 (50.00)| 1 (50.00)|
| Ertapenem                         | 0 (0)    | 5 (100) | 0 (0)   | 2 (100) |
| Cefepime                          | 0 (0)    | 6 (100) | 0 (0)   | 2 (100) |
| Cefotaxin                         | 2 (40.00)| 3 (60.00)| 1 (50.00)| 1 (50.00)|
| Gentamicin                        | 1 (16.67)| 5 (83.33)| 1 (50.00)| 1 (50.00)|
| Imipenem                          | 7 (35.00)| 13 (65.00)| 1 (33.33)| 2 (66.67)|
| Levofoxacin                       | 0 (0)    | 6 (100) | 0 (0)   | 2 (100) |
| Meropenem                         | 0 (0)    | 2 (100) | 0 (0)   | 1 (100) |
| Minocycline                       | 0 (0)    | 1 (100) | 0 (0)   | 1 (100) |
| Piperacillin                      | 1 (100)  | 0 (0)   | 1 (100)  | 0 (0)   |
| Piperacillin/Tazobactam           | 0 (0)    | 6 (100) | 0 (0)   | 2 (100) |
| Trimethoprim/Sulfamethoxazole     | 2 (8.70) | 21 (91.30)| 2 (66.67)| 1 (33.33)|
| Tigecycline                       | 2 (8.70) | 21 (91.30)| 1 (33.33)| 2 (66.67)|
| Clindamycin                       | 3 (15.00)| 17 (85.00)| 2 (100)  | 0 (0)   |
| Erythromycin                      | 4 (21.05)| 15 (78.95)| 2 (100)  | 0 (0)   |
| Habekacin                         | 0 (0)    | 19 (100)| 0 (0)   | 2 (100) |
| Linezolid                         | 0 (0)    | 20 (100)| 0 (0)   | 2 (100) |
| Methicillin                       | 8 (42.11)| 11 (57.89)| 2 (100)  | 0 (0)   |
| Oxacillin                         | 8 (42.11)| 11 (57.89)| 2 (100)  | 0 (0)   |
| Penicillin                        | 18 (94.74)| 1 (5.26) | 1 (100)  | 0 (0)   |
| Teicoplanin                       | 0 (0)    | 20 (100)| 0 (0)   | 2 (100) |
| Tetracycline                      | 6 (30.00)| 14 (70.00)| 0 (0)   | 2 (100) |
| Vancomycin                        | 0 (0)    | 20 (100)| 0 (0)   | 2 (100) |

Values are presented as number (%).
The results of our bacterial culture tests show that the bacteria known to cause soft tissue and skin infections are also associated with HS lesions. The most frequent genus or species isolated were *S. epidermidis*, *S. aureus*, and *E. coli*. The presence of *Staphylococcus lugdunensis* and *Actinomyces europaeus*, which are known to be associated with chronic inflammation, the formation of nodules, and abscess of HS, were also confirmed in this study. The analyses of bacterial susceptibility patterns revealed that among the antibiotics tested in this study, Penicillin, Erythromycin, and Ciprofloxacin were most frequently associated with bacterial resistance. The prevalence of CL resistance was 15.00%. The rates of resistance to CL identified in this study are lower than 65.6% as reported by Bettoli et al. This retrospective study showed that bacterial growth in HS patients has shown a lower level of resistance to CL than that of the previous study, and there was no significant difference in the efficacy of therapy depending on the presence of CL-resistant bacteria before the treatment (p=0.906). CL is a semisynthetic lincosamide antibiotic successor to lincomycin. It inhibits bacterial protein synthesis by binding to bacterial 50S ribosomal subunits. CL may be bacteriostatic or bactericidal depending on the organism and drug concentration. It is active against most anaerobic bacteria and gram-positive cocci except *enterococci*. In this study, we were unable to analyze the therapeutic effect of CL on anaerobic bacteria because our study was limited by the small sample size. Also, CL has the potential to modify or suppress inflammation. It suppresses the complement-derived chemotaxis of polymorphonuclear leukocytes in vitro, reducing inflammation.

The number of patients that experienced adverse events in our study was 14 out of 53 patients (26.42%), which resulted in 9 out of 53 patients (16.98%) to discontinue this regimen. This percentage was higher than that in the study of Caposiena Caro et al., in which the percentage of adverse events of the CL mono-therapy group was 13.3%. However, this percentage was lower than the percentage of adverse events in the RF-CL combination therapy, where the percentage of adverse events was 38.2% and the percentage of patients who stopped therapy due to adverse events was 26.0%. Therefore, it is necessary to consider CL mono-therapy in order reduce side effects as compared to RF-CL combination therapy. The most notable adverse event associated with the use of CL is the development of pseudomembranous colitis by *Clostridium difficile*, one of the patients with diarrhea in our study experienced pseudomembranous colitis. All adverse events ceased after discontinuation of the CL therapy. Therefore, systemic CL is considered a relatively safe treatment. However, if the patient complains of diarrhea after systemic CL therapy, an evaluation may be necessary to differentiate pseudomembranous colitis.

The main limitation of our study is the retrospective study design that failed to draw comparisons against the RF-CL group. Another limitation is that despite the fact that HS frequently recurs and significantly impacts the quality of life, there was no assessment of the recurring episodes and subjective improvement of patients after CL mono-therapy. Prospective randomized controlled trials are needed to confirm these results.

This retrospective study showed that bacterial growth in HS patients has shown a lower level of resistance to CL than that of the previous study, and there was no significant difference in the efficacy of therapy depending on the presence of CL-resistant bacteria. Notably, there was a statistically significant decrease in the HS severity indices after the treatment. These results suggest that systemic CL mono-therapy may be a useful and safe treatment alternative to RF-CL combination, especially in mild to moderate HS patients.

**CONFLICTS OF INTEREST**

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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