Clinical and Experimental Dermatology and Therapies
Ilan V et al. Clin Exp Dermatol Ther 7: 187.
www.doi.org/10.29011/2575-8268.100187
www.gavinpublishers.com

Research Article

Rifampin plus Clindamycin vs. Tetracyclines for Hidradenitis Suppurativa

Vashurin Ilan[1,2]*, Barzilai Aviv[1,2], Baum Sharon[1,2], Zehavi Keren-Or[1,2]

[1]Department of Dermatology, Sheba Medical Center, Ramat-Gan, Israel

[2]Affiliated to the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

***Corresponding author**: Ilan Vashurin, Dermatology Department, Sheba Medical Center, Tel Ha-Shomer, Ramat-Gan, Israel

Citation: Ilan V, Aviv B, Sharon B, Keren-Or Z (2022) Rifampin plus Clindamycin vs. Tetracyclines for Hidradenitis Suppurativa. Clin Exp Dermatol Ther 7: 187 DOI: https://doi.org/10.29011/2575-8268.100187

Received Date: 3 September, 2022; **Accepted Date:** 14 September, 2022; **Published Date:** 18 September, 2022

Abstract

Introduction: Hidradenitis suppurativa (HS) is a chronic, painful, follicular occlusive disease that affects the follicular pilosebaceous unit. It is typically apparent in intertriginous areas, causing abscesses, sinus tract formation, and scarring. Recent guidelines for the management of HS recommend oral treatment with a combination of clindamycin and rifampin for widely spread lesions, although very few studies assessing the efficacy of this combination and its comparison with tetracyclines have been conducted. Hence, this study was aimed at comparatively evaluating the efficacy of the combination of clindamycin and rifampin with that of tetracyclines for the management of HS. **Methods:** We retrospectively evaluated patients diagnosed with HS between 2010 and 2020 at the outpatient dermatology clinics of Sheba Medical Center. The data collected included patients' demographic characteristics (age, sex, and weight); disease stage, including that before, during, and after treatment; treatment period; remission period; flare-ups; treatment failures; and side effects. **Results:** In all, 137 patients including 70 (51.09 %) men and 67 (48.9 %) women were diagnosed with HS; the patients' mean age was 42.4 ± 14.6 years. Among them, 52 patients were treated with a combination of clindamycin and rifampin and 26 were treated with tetracyclines. Thirty-two (61.5 %) and 3 (5.7 %) of the 52 patients treated with clindamycin and rifampin achieved complete and partial remission, respectively. Six of the 26 patients treated with tetracyclines (23 %) achieved complete remission. Tetracyclines were less effective compared to the combination treatment ($p < 0.01$). However, both treatments were less effective against more severe forms of the disease. In the rifampin clindamycin group, the mean remission period was longer (13.6 ± 12.6 months) among those treated for 10 weeks or more. However, the difference in the mean remission period between those treated for 10 weeks or more and fewer than 10 weeks in this group was not significant. Non-smokers showed a better treatment response than that shown by active smokers (complete remission: 73.9 % vs. 51.7 %; $p < 0.01$). **Conclusion:** Treatment with the combination of oral rifampin and clindamycin is effective, mainly against mild-to-moderate HS, and afforded better results than did tetracycline treatment.

Keywords: Hidradenitis suppurativa; Clindamycin; Rifampin; Tetracyclines

Introduction

Hidradenitis suppurativa (HS) is a chronic, painful, follicular occlusive disease that affects the folliculo-pilosebaceous unit in apocrine gland-bearing areas of the body, causing painful abscesses, sinus tract formation, and scarring. The most commonly involved areas in HS are the axillae, groin, and perineum [1-5]. The initial stage of the disease is marked by tender subcutaneous nodules, which may rupture and result in the development of painful, deep dermal abscesses with foul-smelling purulent discharge. As the disease progresses, draining sinus tracts, fibrosis, and scarring could develop [5]. HS is one of the most distressing dermatological diseases, with the Dermatology Life Quality Index in affected patients being 10 ± 8.8 according to recent studies [7,8] and an average prevalence of 1 % in Europe [6]. The disease typically develops between puberty and the age of 40 years, with the usual onset being in the second or third decade of life. Further, women have been found to be more likely to develop HS than men, with the ratio being 3.8:1 [9,10].

The exact etiology of HS is unknown. However, according to the current hypothesis, the disease is multifactorial and possibly triggered by genetic, hormonal, immunological, and environmental factors [5]. Furthermore, smoking and obesity are important risk factors for HS [11-13]. The disease is characterized by sterile inflammation resulting from the primary dysregulation of the immune response in the hair follicle. This results in occlusion and subsequent inflammation of the hair follicle, which can lead to secondary bacterial colonization and infection [5]. Many microorganisms are sporadically associated with the lesions, including *Staphylococcus aureus*, *Streptococcus agalactiae*, anaerobes, and *Corynebacterium* [14].

HS is considered a difficult-to-treat disease, despite the availability of numerous treatment options. Local recurring lesions can be treated using topical medication, surgery, or laser techniques. For widespread lesions, treatment involves pharmaceutical monotherapy or pharmaceutical therapy used in combination with surgical intervention. Pharmaceuticals used for treating HS include a combination of clindamycin and rifampin, tetracyclines, ertapenem, acitretin, cyclosporin A, dapsone, isotretinoin, and biologic agents such as adalimumab or infliximab [6,13]. Lifestyle changes are also an important treatment modality [5].

Recent guidelines for HS management recommend combination antibiotic treatment with clindamycin and rifampin as the conventional treatment modality for HS [6], although the efficacy of this approach has been assessed in very few retrospective studies [1-5]. Clindamycin is a bacteriostatic lincosamide that acts by blocking peptide transfer at the 50S bacterial ribosomal subunit. It has activity against staphylococci, streptococci, pneumococci, and most anaerobic pathogens [15]. In in vitro studies, clindamycin was reported to exert immunomodulatory effects by suppressing bacterial toxin synthesis and reducing inflammation by inhibiting complement-derived chemotaxis of polymorphonuclear leukocytes [16,17]. Rifampin is a semi-synthetic antibiotic that inhibits bacterial DNA-dependent RNA polymerase. It has activity against most gram-positive pathogens, some gram-negative bacteria, and mycobacteria. Furthermore, it can alter the secretion of cytokines by human monocytes [17,18]. Rifampin is highly soluble and can thus sterilize staphylococcal abscesses [1].

Tetracyclines are recommended for the management of mild-to-moderate HS [19]. They interfere with the protein synthesis of susceptible bacteria and possess anti-inflammatory properties. They inhibit enzymes that are active in dermal inflammatory disorders, such as matrix metalloproteinases, hydrolases, and phospholipase A2. Tetracyclines reduce the production of pro-inflammatory cytokines such as TNF-α, IL-1B, IL-6, and IL-8; reduce free radicals; and inhibit angiogenesis and granuloma formation [19,20]. According to Gregor et al., systemic tetracyclines did not show better results than those shown by topical clindamycin in patients with HS [21]. Therefore, in this study, we comparatively assessed the efficacy of clindamycin and rifampin when used in combination with that of tetracyclines for the management of HS.

Materials and Methods

The computerized database at Sheba Medical Center, a tertiary medical center in Israel, was searched for all patients diagnosed with HS who were either admitted to the Department of Dermatology or visited the center's dermatology and plastic surgery outpatient clinics from 2010 to 2020. In all, 137 patients were diagnosed with HS during this period. Among these patients, 66 were treated with a combination of 300 mg rifampin BID and 300 mg clindamycin BID [1-6]. Unfortunately, 14 patients were lost to follow-up; therefore, data were collected for the remaining 52 patients.

Twenty-six patients were treated with tetracyclines (minocycline 100 mg or doxycycline 100 mg once daily). At each follow-up visit, the following data were extracted: disease stage [22,23], treatment period, remission period, flare-ups, treatment failures, and side effects. Disease severity was analyzed before treatment initiation and then approximately every 2 months after treatment initiation by using the Physician's Global Assessment (PGA 1-6) scale. The scores were interpreted as follows: 1 (clear): no inflammatory or non-inflammatory nodules; 2 (minimal): only non-inflammatory nodules; 3 (mild): less than 5 inflammatory nodules or 1 abscess or draining fistula and no inflammatory nodules; 4 (moderate): less than 5 inflammatory nodules, 1 abscess or draining fistula and 1 or more inflammatory nodules, or 2-5 abscesses or draining fistulas and less than 10 inflammatory

nodules; 5 (severe): 2-5 abscesses or draining fistulas and 10 or more inflammatory nodules; 6 (very severe): more than 5 abscesses or draining fistulas [23]. Patients whose PGA score decreased were considered to have achieved complete remission and those whose PGA score was unchanged but showed no signs of inflammation and reported improvement in pain and discharge were considered to have achieved partial remission. Data were analyzed using the chi-square test and Pearson correlation test by using Prism software (ver. 8.4.3) from GraphPad. A significance level of 0.05 was required to validate statistically significant result. The study was approved by the local institutional ethics committee (2999-16-SMC). Written informed consent was not needed.

Results

Between 2010 and 2020, 137 patients (51.09 % men and 48.9 % women) with HS were treated at our center; the mean patient age was 42.4 ± 14.6 years. Among them, 37.9 % were treated with a combination of rifampin and clindamycin and only 18.9 % were treated with tetracyclines at some point. The study sample comprised 78 patients, of whom 52 were treated with the combination of rifampin and clindamycin and 26 with tetracyclines. The demographic characteristics of each group are shown in Table 1. In the combination treatment group, 32 out of 52 (61.5 %) patients achieved complete remission (15 men [55.5 %] and 17 women [68 %]). Three patients (5.7 %) achieved partial remission, and 17 (32.6 %) showed no improvement. In the tetracycline group, only six of the 26 patients achieved complete remission (23 %), and the remaining 20 patients (76.9 %) showed no improvement. Comparison of the two treatments revealed tetracyclines to be less effective ($p < 0.01$) (Figure 1).

Patient characteristics		**Rifampin and clindamycin, n = 52**	**Tetracyclines, n = 26**
Sex	Males	27 (51.9)	13 (50)
	Females	25 (48)	13 (50)
Age (mean ± SD)		38.8 ± 13.8	33.7 ± 10.3
Smokers		29 (55.7)	9 (34.6)
Family history of HS		3 (5.7)	0
BMI (mean ± SD)		28 ± 7.6	25.4 ± 5.9
Area involved	Axillae	26 (50)	11 (42.3)
	Breast folds	8 (15.3)	1 (3.8)
	Groin	43 (82.6)	18 (69.2)
	Gluteal	24 (46.1)	12 (46.1)
	Genitals	7 (13.4)	3 (11.5)
	Other sites	11 (21.1)	7 (26.9)
Disease severity	Mild	4 (7.6)	6 (23)
	Moderate	32 (61.5)	15 (57.6)
	Severe	16 (30.7)	5 (19.2)
Positive culture from lesions		27 (51.9)	5 (19.2)
Hospitalization as a result of flares		22 (42.3)	6 (23)
Other treatment modalities	Retinoids	30 (57.6)	0
	Biologics	13 (25)	0
	Drainage	24 (46.1)	13 (50)
	Surgical removal	23 (44.2)	8 (30.7)
Side effects due to treatment		9 (17.3)	2 (7.6)

(Numbers in parentheses are percentages)

Table 1: Descriptive characteristics of the patients

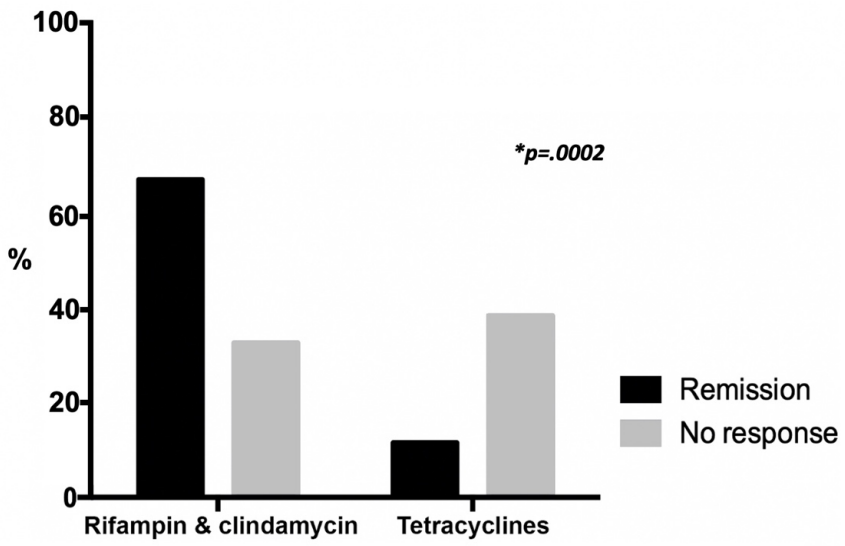

Figure 1: Remission rate in the rifampin plus clindamycin and tetracycline groups, $p < 0.01$.

In the combination treatment group, the outcomes were better for mild and moderate disease. Complete remission was achieved in 100 % and 68.7 % of the patients with mild and moderate disease, respectively. Partial remission was achieved in 6.2 % of the patients with moderate disease. Among those with severe disease, 37.5 % and 6.2 % of the patients achieved complete and partial remission, respectively (Table 2). Regarding age, among the 35 patients who achieved complete and partial remission, 22 (62.8 %) aged less than 40 years and 13 (37.1 %) patients were 40 years or higher.

Group	Disease severity		Complete remission	Partial remission	No improvement
Rifampin and clindamycin	Mild	n = 4	4 (100)	-	-
	Moderate	n = 32	22 (68.7)	2 (6.2)	8 (25)
	Severe	n = 16	6 (37.5)	1 (6.2)	9 (56.2)
Tetracyclines	Mild	n = 6	4 (66.6)	-	2 (33.3)
	Moderate	n = 15	2 (13.3)	-	13 (86.6)
	Severe	n = 5	-	-	5 (100)

Table 2: Treatment outcomes according to disease staging

Regarding the duration of treatment and remission, 20 patients were treated for less than 10 weeks, with the mean treatment duration being 6.2 ± 1.9 weeks in these patients, and 32 patients were treated for 10 or more weeks, with the mean treatment duration being 18.3 ± 12.6 weeks in these patients. Regarding remissions, 60 % and 62.5 % were achieved remission with less than 10 weeks of treatment and treatment for 10 weeks or more, respectively. Among the 35 patients who responded to treatment, 34.2 % and 65.7 % were treated for less than 10 weeks and for 10 or more weeks, respectively. However, the mean time to treatment response was 8.1 ± 4.2 weeks. The average remission period in cases of patients for whom the treatment duration was shorter and longer were 6.8 ± 7.5 and 13.6 ± 12.6 months, respectively (Table 3). There was no significant correlation between treatment duration and remission period ($p = 0.07$) (Fig. 2). In addition, there was no significant correlation between disease severity and time to response. Moreover, no significant differences were found between body mass index (BMI), site of disease involvement, and time to response.

Tx Duration		Complete remission	Partial remission	No improvement	Mean Tx period (weeks ± SD)	Remission period (mean months ± SD)	P value
Dosage: Clindamycin 300 mg BID + Rifampin 300 mg BID							
<10 weeks	n = 20	12 (60)	-	8 (40)	6.2 ± 1.9	6.8 ± 7.5	
Mild	n = 1	1 (100)	-	-			
Moderate	n = 13	8 (61.5)	-	5 (38.4)			
Severe	n = 6	3 (50)	-	3 (50)			
≥10 weeks	n = 32	20 (6.5)	3 (9.3)	9 (28.1)	18.3 ± 12.6	13.6 ± 12.6	
Mild	n = 3	3 (100)	-	-			
Moderate	n = 19	14 (73.6)	2 (10.5)	3 (15.7)			
Severe	n = 10	3 (30)	1 (10)	6 (60)			p=.3745

(Numbers in parentheses are percentages)

Table 3: Outcomes in the combination rifampin and clindamycin group according to the duration of treatment and remission periods.

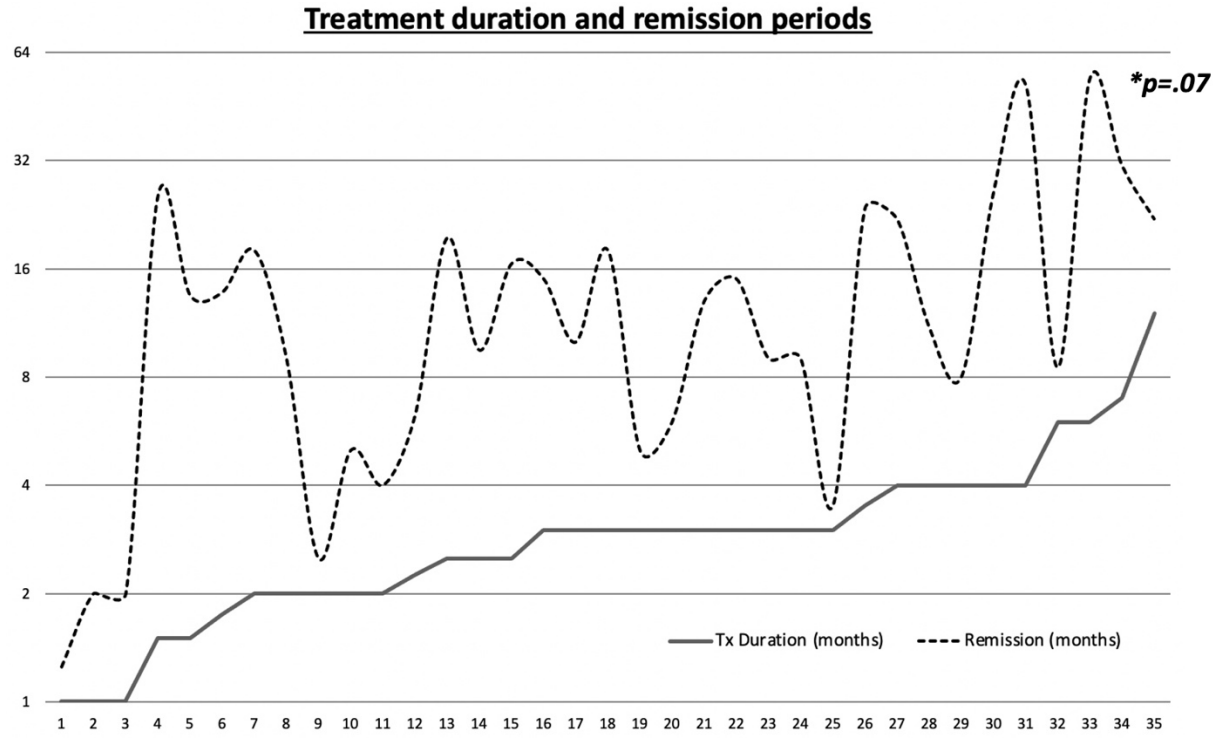

Figure: 2 Outcomes according to duration of treatment and remission periods in the rifampin plus clindamycin group.

There were 30 obese patients (57.6 %) and 29 active smokers (55.7 %). Upon classifying the patient according to BMI and smoking status, we found that 18 obese patients (60 %) and 15 smokers (51.7 %) achieved complete remission, and one obese patient (3.3 %) achieved partial remission (Table 4). There was a significant association between smoking and treatment efficacy ($p < 0.01$), and no significance was observed between BMI and treatment efficacy ($p = 0.9$). Smokers had longer periods of remission that were significant ($p < 0.05$). Among the responders, 48.5 % had normal BMI and 57.1 % were non-smokers.

Smoking status		Complete remission	Partial improvement	No improvement	Mean duration until improvement (weeks)	P value
Active smoker	n = 29	15 (51.7)	-	14 (48.2)	7.2 ± 4.5	p=.007
Non-smoker	n = 23	17 (73.9)	3 (13)	3 (13)	8.8 ± 4.04	

(Numbers in parentheses are percentages)

Table 4: Results of combination treatment with rifampin and clindamycin according to patients' smoking status.

Most patients showed involvement of more than one body site. Forty-three patients showed groin involvement, and among them, 26 (60.4 %) and 2 (4.6 %) patients achieved complete and partial remission, respectively. Among 25 patients with axillary lesions, 16 (64 %) and 2 (8 %) achieved complete and partial remission, respectively. Among the 24 patients with gluteal lesions, 15 (62.5 %) had complete remission and 1 (4.1 %) had partial remission. Among the eight patients with breast fold lesions, seven patients (87.5 %) had remission. Only three patients with genital lesions (42.8 %) achieved remission. The remaining 11 patients showed involvement of other less common involved body areas (such as the neck, back, and others), and 7 (63.6 %) of these patients achieved remission. Thirty-three patients had involvement of two or fewer body sites; among them, 19 (57.5 %) and 3 (9 %) achieved complete and partial remission, respectively. Nineteen patients showed involvement of more than two body sites; among them, 13 patients (68.4 %) achieved complete remission. There was no significant association between the site of involvement and treatment efficacy ($p = 0.89$).

In the tetracycline group, 66.6 % of the patients with mild disease and 13.3% with moderate disease achieved complete remission (Table 2). Among the six patients who achieved complete remission, 4 (66.6 %) were aged less than 40 years and two (33.3 %) were aged 40 years or higher. The mean treatment and remission periods for these patients were 2.08 ± 1.3 and 15.1 ± 7.2 months, respectively. Among those who achieved complete remission, 83.3 % were non-smokers and 66.6 % had a normal BMI. Among those who did not respond to treatment, 40 % and 60 % were smokers and non-smokers, respectively. Furthermore, 45 % and 55 % of these patients had a high and normal BMI, respectively, with no significant correlations between treatment duration, smoking, BMI and remission.

Discussion

In this study, we comparatively assessed the efficacy of rifampin and clindamycin combination treatment and tetracyclines for the treatment of HS. Among 66 patients who were treated with a combination of rifampin and clindamycin, 14 were lost to follow-up; therefore, they were not included in the final analysis. Twenty-six patients were treated with tetracyclines. In our study population, patients presented with the disease mostly in the third decade of their lives, similar to that reported previously. The body sites that were mostly involved were the axillae and groin [1-5]. However, in contrast to that previously reported in the literature, there was no sex predominance in our study [9,10].

Our results revealed that the combination treatment was significantly more effective than the tetracycline treatment ($p < 0.01$), with 61.5 % of those treated with the former achieving complete remissions. Our results are similar to those of the studies by Mendonca, Van der Zee, Gener, and Bettoli [1-4]. On the other hand, only 23 % of the patients treated with tetracyclines achieved complete remission. These findings contrasted with the finding of a recent study [24] that showed significant efficacy of tetracyclines and combination rifampin and clindamycin with no significant differences between these two treatments. Further, in both of our study groups, the treatment was less effective when the disease was more severe, and a small number of patients had mild disease. Undoubtedly, this result could be even more pronounced in a larger number of patients with mild disease.

Based on guidelines and previously published literature [1-5], treatment with rifampin plus clindamycin is usually administered for only 10 weeks due to concerns about toxicity from long-term treatment. In this study, 20 patients were treated for less than 10 weeks, and 32 patients were treated for 10 or more weeks. Patients who were treated for 10 or more weeks achieved complete remission (62.5 %) or partial remission (9.3 %) with mean remission period of 13.6 ± 12.6 months. Among, those who were treated for less than 10 weeks, 60 % of the patients showed a treatment response, and these patients had a shorter remission period, with the mean duration being 6.8 ± 7.5 weeks. However, the difference in the mean remission period between the patients treated for 10 or more weeks and those treated for less than 10 weeks was not significant, and the remission period appears almost the same for the two groups (Fig. 2). According to Van der Zee et al. [2], the response rate is even lower among those treated for 10 or more weeks. It seems that larger studies must be performed to assess the response rate and treatment duration.

Eight patients who received the combination treatment developed side effects, with the most common ones being diarrhea, epigastric pain, malaise, and elevated liver enzyme levels. No cases of clindamycin-related *Clostridium difficile* colitis were observed, and there was no treatment discontinuation because of side effects. Furthermore, there was no increase in side effects among those treated for more than 10 weeks. Only two patients who were treated with tetracyclines developed side effects. One patient was treated with doxycycline and the other with minocycline, and both reported weakness.

Garg and Canoui-Poitrine [9,10] have shown that women are more likely to develop HS. The entire population sample of our study consisted of 67 women and 70 men. Among those treated with rifampin and clindamycin, women showed a better treatment response than did men (76 % and 59.2 %, respectively) but the difference was not significant ($p = 0.19$). One hypothesis is that women have better compliance than men [25]. Younger patients (age less than 40 years) were found to be more responsive to treatment (78.5 %) than were older patients (54.1 %), $p = 0.06$).

Smoking and obesity are considered important risk factors for HS development. In our study, non-smokers were found to have a better treatment response than did active smokers (complete remission: 73.9 % vs. 51.7 %; $x^2 = 7.23$, $p < 0.01$). Nicotine and other chemicals in tobacco smoke enhance the inflammatory cascade in HS pathogenesis by inducing the production of pro-inflammatory cytokines by keratinocytes, proliferation of *Staphylococcus aureus*, and enhancement of the virulence of other bacteria [26]. Smokers had longer periods of remission than did non-smokers: 14.5 ± 12.44 months vs. 8.9 ± 10.49; $x^2 = 4.89$, $p < 0.05$. Cigarette smoke reduces neutrophil defense and inflammatory responses [27]. This explains why smokers had longer periods of remission. The remission period was almost the same between obese and non-obese patients, and the intergroup difference was not significant.

Lesion sites differed among patients, and patients with the involvement of breast folds tended to be more responsive to treatment with rifampin and clindamycin (87.5 %) compared to those with the involvement of other body sites ($p = 0.89$). In our cohort, only three patients had a family history of HS. Cultures from the lesions were obtained from 32 patients with polymicrobial growth. These findings did not have a significant impact on treatment efficacy. Among 17 patients who did not respond to treatment, 52.9 % underwent surgical excision, and biologic medications (adalimumab or apremilast) were administered to the rest.

It is posited that the efficacy of the rifampin plus clindamycin combination is attributable to the antibacterial and anti-inflammatory properties of these two antibiotics. Clindamycin has good activity against gram-positive and anaerobic microorganisms. It suppresses bacterial toxin synthesis and complement-derived chemotaxis of leukocytes, which decreases inflammation [15,28]. Rifampin has great activity against *Staphylococcus aureus* and suppresses the antigen-induced transformation of sensitized lymphocytes, which decreases cell-mediated hypersensitivity. Furthermore, it is highly soluble and can sterilize staphylococcal abscesses [1,28].

This study has a few limitations. This was a retrospective study with a relatively small cohort of patients. Furthermore, the patients were observed by different physicians; therefore, inter-observer expectancy bias is likely. Thus, larger, double-blinded, prospective studies are needed to confirm the efficacy of rifampin plus clindamycin combination treatment and it's comparison to tetracyclines.

In conclusion, the combination of rifampin and clindamycin was found to be more effective than tetracyclines for the treatment of HS. Furthermore, the combination treatment was more effective in patients with mild and moderate disease. Lastly, smoking was found to be an important factor that decreased treatment efficacy, and no significant difference was found between the duration of treatment and remission.

Author Contributions

V.I. and Z.K. conceptualized the study including data collection and performing the statistical analysis. A revision of the manuscript was performed by B.A. and B.S. All authors contributed to the accomplishment of the manuscript by reading and continually improving it.

References

1. Mendonça CO, Griffiths CE (2006) Clindamycin and rifampicin combination therapy for hidradenitis suppurativa. Br J Dermatol 154:977–978.
2. Van der Zee HH, Boer J, Prens EP, Jemec GB (2009) The effect of combined treatment with oral clindamycin and oral rifampicin in patients with hidradenitis suppurativa. Dermatology 219:143–147.
3. Bettoli V, Zauli S, Borghi A, Toni G, Minghetti S, Ricci M, et al. (2014) Oral clindamycin and rifampicin in the treatment of hidradenitis suppurativa-acne inversa: a prospective study on 23 patients. J Eur Acad Dermatol Venereol 28:125–126.
4. Gener G, Canoui-Poitrine F, Revuz JE, Faye O, Poli F, Gabison G et al. (2009) Combination therapy with clindamycin and rifampicin for hidradenitis suppurativa: a series of 116 consecutive patients. Dermatology 219:148–54.
5. Napolitano M, Megna M, Timoshchuk EA, Patruno C, Balato N, et al. (2017) Hidradenitis suppurativa: from pathogenesis to diagnosis and treatment. Clin Cosmet Investig Dermatol 10: 105–115.
6. Zouboulis CC, Desai N, Emtestam L, Hunger RE, Ioannides D, Juhász I, et al. (2015) European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. J Eur Acad Dermatol Venereol 29:619–644.

7. Wolkenstein P, Loundou A, Barrau K, Auquier P, Revuz J (2007) Quality of Life Group of the French Society of Dermatology. Quality of life impairment in hidradenitis suppurativa: a study of 61 cases. J Am Acad Dermatol 56:621–623.

8. Alavi A, Anooshirvani N, Kim WB, Coutts P, Sibbald RG (2015) Quality-of-life impairment in patients with hidradenitis suppurativa: a Canadian study. Am J Clin Dermatol 16:61–65.

9. Garg.A, Lavian J, Ling G et al. (2017) Incidence of hidradenitis suppurativa in the United States: A sex- and age-adjusted population analysis. J Am Acad Dermatol 153:760-764

10. Canoui-Poitrine F, Le Thuaut A, Revuz JE, Viallette C, Gabison G, Poli F, et al. (2013) Identification of three hidradenitis suppurativa phenotypes: latent class analysis of a cross-sectional study. J Invest Dermatol 133:1506–1511.

11. Vazquez BG, Alikhan A, Weaver AL, Wetter DA, Davis MD (2013) Incidence of hidradenitis suppurativa and associated factors: a population-based study of Olmsted County, Minnesota. J Invest Dermatol 133:97–103.

12. Schrader AM, Deckers IE, van der Zee HH, Boer J, Prens EP (2014) Hidradenitis suppurativa: a retrospective study of 846 Dutch patients to identify factors associated with disease severity. J Am Acad Dermatol 71:460–467.

13. Lee EY, Alhusayen R, Lansang P, Shear N, Yeung J (2017) What is hidradenitis suppurativa? Can Fam Physician 63:114–120.

14. Guet-Revillet H, Coignard-Biehler H, Jais JP, Quesne G, Frapy E, Poirée S et al. (2014) Bacterial pathogens associated with hidradenitis suppurativa, France. Emerg Infect Dis 20:1990–1998.

15. Smieja M (1998) Current indications for the use of clindamycin: A critical review. Can J Infect Dis 9:22–28.

16. Pasquale TR, Tan JS (2005) Non antimicrobial effects of antibacterial agents. Clin Infect Dis 40:127–135.

17. Pradhan S, Madke B, Kabra P, Singh AL (2016) Anti-inflammatory and immunomodulatory effects of antibiotics and their use in dermatology. Indian J Dermatol 61:469–481.

18. Schonell M, Dorken E, Grzybowski S (1972) Rifampin. Can Med Assoc J 106 :783–786.

19. Frew JW, Jason E. Hawkes ans James G. Krueger (2019) Topical, systemic and biologic therapies in hidradenitis suppurativa: pathogenic insights by examining therapeutic mechanisms. Ther Adv Chronic Dis 10:1–24.

20. Sun J, Shigemi H, Tanaka Y, Yamauchi T, Ueda T, Iwasaki H (2015) Tetracyclines downregulate the production of LPS-included cytokines and chemokines in THP-1 cells via ERK, p38 and nuclear factor kB signaling pathways. Biochem Biophys Res 4:397–404.

21. Jemec GBE, Wendelboe P (1998) Topical clindamycin versus systemic tetracycline in the treatment of hidradenitis suppurativa. J Am Acad Dermatol 39:971–974.

22. Dufour DN, Emtestam L, Jemec GB (2014) Hidradenitis suppurativa: a common and burdensome, yet under-recognised, inflammatory skin disease. Postgrad Med J 90:216–221.

23. Pascoe VL, Enamandram ME, Corey KC, Cheng CE, Javorsky EJ, Sung SM. et al. (2015) Using the physician global assessment in a clinical setting to measure and track patient outcomes. JAMA Dermatol 151:375–381.

24. Van Straalen KR, Tzellos T, Guillem P, Benhadou F, Cuenca-Barrales C, Daxhelet M, et al.(2021) The efficacy and tolerability of tetracyclines and clindamycin plus rifampicin for the treatment of hidradenitis suppurativa; results of a prospective European cohort study. J Am Acad Dermatol S0190–9622:00176–6.

25. Manteuffel M, Williams S, Chen W, Verbrugge RR, Pittman DG, Steinkellner A (2014) Influence of patient sex and gender on medication use, adherence, and prescribing alignment with guidelines. J Womens Health (Larchmt) 23:112–119.

26. Bukvić Mokos Z, Miše J, Balić A, Marinović B (2020) Understanding the relationship between smoking and hidradenitis suppurativa. Acta Dermatovenerol Croat 28:9–13.

27. Zhang Y, Geng S, Prasad GL, Li L G. L et al. (2018) Suppression of neutrophil antimicrobial functions by total particulate matter from cigarette smoke. Front Immunol 9:2274.

28. Harumi O, Lixian C. T, Hazel H. O (2018) The effect of oral clindamycin and rifampin combination therapy in patients with hidradenitis suppurativa in Singapore. Clin Cosmet Investig Dermatol 11:37–39.