HHS Public Access

Author manuscript

Am J Clin Dermatol. Author manuscript; available in PMC 2022 May 25.

Published in final edited form as:

Am J Clin Dermatol. 2022 March ; 23(2): 167–176. doi:10.1007/s40257-021-00667-8.

Medical Management of Hidradenitis Suppurativa with Non-Biologic Therapy: What's New?

Soha Ghanian[1], **Mika Yamanaka-Takaichi**[2], **Haley B. Naik**[3], **Afsaneh Alavi**[2]

[1]Department of Dermatology, The Warren Alpert Medical School of Brown University, Providence, RI, USA

[2]Department of Dermatology, Mayo Clinic, Rochester, MN, USA

[3]Department of Dermatology, University of California San Francisco, San Francisco, CA, USA

Abstract

Hidradenitis suppurativa (HS) is a severe chronic relapsing inflammatory disorder of the hair follicle unit that can cause painful abscesses, nodules, tunnels, and tracts in intertriginous parts of the body. The disease can often result in disfigurement and adversely impact patient quality of life. The management of HS has expanded significantly over the past decade to include multiple modalities, including topical therapies, systemic therapies (non-biologics and biologics), surgical therapies, lifestyle changes, and management of comorbidities. Management can often be clinically challenging and may involve the combination of medical and surgical approaches for optimal results. The purpose of this review is to present an update on non-biologic and non-interventional modalities published in 2019–2021 in the clinical management of HS. With emerging therapies, ongoing clinical trials, and heightened awareness about HS, there is hope that new treatment options will revolutionize the management of patients suffering from HS.

1 Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory disorder involving intertriginous areas. Inflammation in patients with HS is not restricted to the skin but is systemic, affecting several other organs [1]. Patients with HS are not only affected by recurrent painful draining skin lesions but also with associated comorbidities, including, but not limited to, metabolic syndrome and mood disorders [2, 3]. The earlier implementation of proper treatment is associated with better outcomes. Not uncommonly, patients with HS are faced with late diagnosis and undertreatment, and in dermatology we face patients suffering from both inflammation and fibrosis. The management of HS requires multiple modalities and a team approach to include the management of inflammation (amenable to medical treatment), scarring (amenable to surgery). and comorbidities (to involve a multidisciplinary approach). Biologics remain the treatment of choice for moderate to severe disease and

Afsaneh Alavi, alavi.afsaneh@mayo.edu.

Author contributions SG and MYT performed the literature review, and MYT, HBN, and AA edited the manuscript.

Conflicts of interests/Competing interests Soha Ghanian, Mika Yamanaka-Takaichi, and Haley B. Naik have no conflicts of interest to disclose. Afsaneh Alavi is a consultant for Abbvie, Boehringer Ingelheim, Janssen, InflaRx, Novartis, and UCB.

surgical intervention is the treatment of choice for addressing permanently damaged tissue. There remains an adjunctive role for non-biologic therapies to be used in conjunction with biologics and surgical interventions in moderate to severe disease or as monotherapy for mild disease. Even though approval of the first anti-tumor necrosis factor (TNF) inhibitor in the management of HS shed light on this disease, with many more targeted therapies currently in the pipeline [4, 5], non-biologic therapies play a key role in managing HS [6]. We searched PubMed for studies and selected case reports from 2019 to 2021 for the current non-biologic therapies, which encompass antimicrobial, hormonal, anti-inflammatory, and retinoid drugs. This paper provides an update on the medical management of HS (excluding biologics and Janus kinase (JAK) inhibitors and phosphodiesterase inhibitors). A summary of recently published studies of these agents can be found in Table 1.

2 Antimicrobial Washes

The use of antiseptic washes in the management HS is supported by anecdotal evidence. Chlorhexidine wash, bleach baths, pyrithione zinc shampoo, and benzoyl peroxide (BPO) are commonly used in the management of HS as adjunctive therapy for their anti-inflammatory properties and ability to reduce antibacterial resistance [7-9]. Choice of specific agent is often empiric and guided by expert opinion [10]. A cross-sectional study looking at adherence to antimicrobial washes use among HS patients found that 30% of the 54 patients who had been recommended to use washes were using them on a daily basis, which raises questions about the practicality of whole-body washes and barriers to accessing washes [11].

3 Topical Therapies

Current North American clinical management guidelines for HS support clindamycin use in HS [10]. The use of topical antibiotics such as clindamycin is associated with a high risk of bacterial resistance, as shown in one cross-sectional study, which showed that HS patients using topical clindamycin were more likely to grow clindamycin-resistant *Staphylococcus aureus* [12]. For this reason, concomitant use of antiseptic washes, such as BPO, are recommended to help reduce resistance.

The efficacy of topical ichthammol 10% ointment, also known as ammonium bituminosulfonate, which is prepared by distillation of bituminous shale and ammonium sulfate, in HS patients has been reported [13]. Ichthammol is suggested as a local treatment in the Swiss practice recommendations for the management of HS [14]; however, these results are based largely on case series and expert opinion.

Resorcinol 15% cream, a compound structurally similar to phenol, with keratolytic, antimicrobial, and anti-inflammatory properties, is also used in the management of HS. In a case series studying the efficacy of topical resorcinol treatment among patients with stage I–II HS, all patients self-reported a reduction in pain from nodules [15]. In one study conducted by Molinelli et al., there was a significant reduction in mean pain and size and number of nodules and abscesses after treatment with topical 15% resorcinol cream [16]. Another study reported that HS patients treated with resorcinol 15% were satisfied

with the treatment and 84.8% of patients responded to a questionnaire that they would recommend this treatment [17]. These studies suggest the long-term safety and efficacy of topical resorcinol use in the management of mild-to-moderate HS, although resorcinol is not available as a commercial formulation in the US and has to be compounded by a pharmacist.

4 Intralesional and Systemic Steroids

Recent studies provide more evidence for the use of intralesional steroids for flares and localized active lesions [18]. Intralesional corticosteroid therapy is an option for isolated HS nodules, likely through activation of intralesional glucocorticoid receptors and subsequent blockage of proinflammatory cytokine production [19, 20]. However, in a recent randomized controlled trial comparing intralesional triamcinolone and normal saline (NS), there was no statistically significant difference between the two concentrations of triamcinolone and NS in the treatment of acute HS lesions, although a low concentration of intralesional steroid (0.1 mL) was delivered to each inflammatory lesion [21].

In an interventional prospective study looking at the treatment of HS using intralesional ultrasound-guided triamcinolone plus lincomycin injections at baseline and at 2 weeks, there was a statistically significant improvement in pain, clinical improvement, and overall patient satisfaction at the week-4 follow-up [22]. In a follow-up study conducted by Caposiena Caro et al., there was also a statistically significant improvement in moderate–severe HS patients who were treated with intralesional ultrasound-guided triamcinolone and lincomycin injection. These studies offer promising hope for the use of intralesional corticosteroid injections in conjunction with an antibiotic in the management of acute HS flares and as a neoadjuvant therapy prior to surgery [23, 24]. García-Martínez et al. reported that high-frequency cutaneous ultrasound examination prior to intralesional corticosteroid injection improved clinical outcomes in all lesion types, including fistulous tracts and fluid collections [25].

In an interesting case of recalcitrant Crohn’s disease and Hurley stage III HS, tumescent anesthesia and 120 mg of triamcinolone in the form of a 40 mg/mL solution mixed into a saline bag were prepared and delivered intralesionally with significant clinical improvement 48 h after the procedure, with sustained results for 7 months after the procedure. Further studies are needed to study the efficacy and practicality of this drug delivery method for the treatment of recalcitrant HS [26]. In a recent study, the effectiveness of adjunctive therapy with systemic or intralesional corticosteroids to adalimumab among 38 patients with stage II-III HS with recurrence on biologics was evaluated. After stratification of the patients into two treatment arms (intralesional methylprednisolone, and oral prednisone), 88% of patients in the oral prednisone group and 85% of patients in the intralesional group showed improvement in the International Hidradenitis Suppurativa Severity Score System (IHS4), Dermatology Life Quality Index (DLQI), and pain visual analog scale (VAS) [27]. This demonstrates the importance of considering combination therapy, especially for managing acute HS flares.

5 Antibiotic Therapy

Systemic antibiotics are the first line of therapy in HS. HS lesions are colonized by bacteria, and biofilms have been found in the tunnels of HS lesions. Antibiotic therapy is often used due to both its antimicrobial and anti-inflammatory properties [28]. A case-control study comparing the skin microbiome of HS patients and healthy controls revealed variation in the amount and type of bacteria according to HS severity and lesion morphology, with dominant bacteria within HS lesions including *Actinobacter* and *Moraxella* species, *Staphylococcus epidermidis,* and anaerobes such as *Porphyromonas* and *Peptoniphlius* species, and a significantly higher abundance of *Propionibacterium acnes* in healthy controls, suggesting reduced *Proprionibacterium* colonization could contribute to HS pathogenesis [29].

In a recent study looking at the duration of antibiotic treatment, the authors found that the majority of oral antibiotic courses for HS have durations of < 12 weeks in an attempt to avoid emergence of antibiotic resistance [30]. Systemic tetracycline antibiotics, often used as first-line treatment for Hurley stage I and II HS, work by blocking the 30S subunit of the bacterial ribosome and also by blocking cytokine production. Common tetracycline antibiotics used for HS management include tetracycline 500 mg twice daily, doxycycline 100 mg twice daily, and minocycline 100 mg once daily [31] One study demonstrated the efficacy of combination therapy with colchicine and minocycline in HS [32]. In a recent Danish study evaluating the clinical efficacy of tetracycline, doxycycline, and lymecycline for the management of 108 HS patients, the greatest clinical improvement was observed in the tetracycline treatment group. Furthermore, response to treatment was significantly associated with lower body mass index (BMI), Hurley stage III, higher disease severity at baseline, and higher number of boils in the preceding month at baseline. Moreover, almost all secondary outcomes, including quality of life, overall disease-related distress, and number of boils in the preceding month, improved significantly in all groups [33].

Clindamycin, an antibiotic with anti-*staphylococcal* and anti-*streptococcal* coverage that works by inhibiting bacterial protein synthesis and suppressing neutrophil chemotaxis, is also used in the management of HS [34]. Rifampicin, a broad-spectrum antibiotic, can also be used in HS management for both its antimicrobial and immunomodulatory properties [34, 35]. The clindamycin/rifampicin combination has been well-studied in the management of HS with favorable success rates, especially in less-severe disease [36]. One study of 54 patients receiving oral clindamycin 300 mg and rifampicin 300 mg twice daily reported that a total 80% of the patients showed improvement in Hidradenitis Suppurativa Score (HSS) to some extent, including 37% achieving an improvement in HSS of ≥ 50% from baseline and 13% achieving full remission (100% improvement in HSS) at the 6-month follow-up. Conversely, 11% of the patients showed worsening in disease and 9% showed no change in HSS or were lost to follow-up. In this study, adverse effects were reported by 56% of the patients and the most commonly occurring adverse effect was diarrhea (12 patients, 22%) [37]. One study of 20 pediatric patients treated with a 10-week combination of oral clindamycin and rifampicin found that 60% of patients achieved a Sartorius score improvement ≥ 50% [38]. In a recent prospective, cohort study assessing the 12-week efficacy of oral tetracyclines (tetracycline, doxycycline, and minocyline) and a clindamycin/rifampicin combination, there was a significant reduction in the IHS4 from baseline among

patients in both treatment groups. Interestingly, no significant difference was observed between patients in the two treatment groups, regardless of the disease severity [39]. A 52-patient retrospective study showed that lymecycline monotherapy and clindamycin plus rifampicin combination are both effective treatments for patients with moderate–severe HS. This study suggests that nodular-type HS may respond better to lymecycline, whereas the abscess/tunnel type may respond better to clindamycin plus rifampicin [40].

In another study evaluating the efficacy of oral clindamycin versus that of a clindamycin/rifampicin combination among 60 HS patients, both groups had a similar, statistically significant improvement in IHS4 scores, possibly indicating that clindamycin alone may be a useful treatment, regardless of disease severity [41]. A retrospective study of 31 HS patients treated with oral clindamycin showed a mean Sartorius score reduction of 42.5% and complete remission in three patients. The severity of HS increased in only one patient, which also indicates the efficacy of oral clindamycin monotherapy compared with the rifampicin/clindamycin combination in a selected group of patients [42]. Although the efficacy of clindamycin against HS has been shown, it should be noted that the use of clindamycin carries the highest risk of community-associated *Clostridium difficile* infection, and combination with rifampin reduces the risk [43].

One prospective cohort study with 28 patients showed the efficacy of the oral combination of rifampin, moxifloxacin, and metronidazole (RMoM) in patients with severe Hurley stage HS. The median Sartorius score dropped from 14 to 0 at week 12, with 75% of patients reaching clinical remission [44].

Metronidazole, an antimicrobial agent with strong anaerobic coverage against *Prevotella* and *Porphyromonas* species and immunomodulatory effects of T cells, has also been studied in the management of HS [29]. Treating patients with Hurley stage I and II HS with metronidazole 500 mg three times daily for 2 weeks may be helpful in reducing anaerobic bacterial load, especially *Prevotella,* which is resistant to clindamycin [30]. Topical metronidazole may be more effective than clindamycin in the eradication and prevention of colonization by *Prevotella* and *Porphyromonas* species and may possess a more robust anti-inflammatory profile, although this has yet to be studied in HS [45].

Ertapenem is a broad-spectrum carbapenem antibiotic used intravenously for the treatment of skin and soft tissue infections and HS [46]. In a retrospective study of 30 patients with severe HS treated with ertapenem for 6 weeks, disease relapse was common after treatment cessation. Ertapenem might be used to achieve rapid improvement of disease as a bridge to surgery or other maintenance therapies, such as biologic therapy, in order to prevent relapses [47, 48].

Dapsone is a sulfone drug with antimicrobial, bacteriostatic, and anti-inflammatory properties that can be used for Hurley stage I and II HS. In a retrospective study of 24 HS patients treated with dapsone, clinical improvement was seen in 38% of patients, suggesting that dapsone therapy may be possible for mild HS, but that rapid recurrence after treatment cessation is a concern [49]. In a recent study looking at 25 patients with mild-to-moderate disease, there was clinical improvement in 64% of patients and no clinical improvement in

patients with Hurley stage III HS. In spite of the decreased efficacy with dose reduction, dapsone can serve as an option for stage I–II HS while bridging to maintenance therapy [50].

Despite the extensive use and evidence on efficacy of antibiotics, the emergent evidence on bacterial resistance limits the use of these treatments.

6 Hormonal Therapies

Androgen and estrogen levels play a role in HS, as patients may often experience premenstrual flares. HS is more common in women of child-bearing age, with the incidence dropping after menopause [51, 52]. Small sample sizes, variable outcome measures and methods, and reporting bias all limit the evidence for the use of hormonal therapy in HS [52]. The only reported randomized controlled, double-blinded, crossover trial of hormonal therapy in HS compared ethinylestradiol/noregestrol on days 5–25 of the menstrual cycle with ethinylestradiol on days 5–25 and cyproterone acetate on days 5–14 of the menstrual cycle. Both groups had decreased plasma testosterone levels and similar improvement in HS, but there was no clinically significant difference between the two treatment groups [53].

Spironolactone is a potassium-sparing diuretic that exerts anti-androgen properties through its ability to block mineralocorticoid receptors [54]. In a retrospective study on oral spironolactone (75 mg daily), there was a statistically significant improvement in pain score, number of inflammatory lesions, and Physician Global Assessment (PGA) score, indicating that anti-androgen therapy may be useful in the management of HS among females who report menstrual flares [52, 55]. A retrospective chart review of 26 women patients taking spironolactone 100 mg or 50 mg daily revealed it was well-tolerated and effective, with a reduction in DLQI of >5, however further studies are needed to identify optimal dosing and efficacy [56].

Metformin is an antihyperglycemic agent that improves insulin receptor sensitivity and reduces insulin resistance through improved glucose uptake, and may also possess anti-androgen properties. Since HS patients may have hyperandrogenism, co-occurring polycystic ovarian syndrome (PCOS), and low glucose tolerance, metformin is another treatment option. In a retrospective study of Hurley stage I–III HS patients treated with metformin, clinical response was seen in 68% of patients, with the majority being stage II patients [57]. In another study, 75% of patients had features of insulin resistance, but this did not predict response to treatment [58]. One retrospective chart review with 16 pediatric HS patients treated with metformin as adjunctive therapy showed improvement in five patients with decreased frequency of flares, whereas five patients had no improvement. Six patients were lost to follow-up or data were not available [59].

Overall, hormonal agents are considered a good therapeutic option in females with HS who report menstrual flares or who have features of PCOS [60].

7 Retinoid Therapy

Retinoids have been historically used for HS, likely due to similarities between HS and acne vulgaris pathogenesis [61]. Results from isotretinoin studies have been mixed. In a recent

retrospective study of 209 HS patients with a prior history of isotretinoin use, no response to treatment was reported among 64.1% of patients. Responders were more likely to have a history of pilonidal cysts than non-responders. Having a concomitant history of acne did not enhance HS treatment response to isotretinoin [62]. In another retrospective study of 31 HS patients, combination therapy with isotretinoin and adalimumab led to a positive clinical response [63]. Acitretin is a retinoic acid derivative often used in the management of psoriasis that works by inhibiting epidermal growth and differentiation [64]. In addition to disorders of keratinization, it may be useful for the management of nodulocystic acne and HS that are not adequately suppressed by isotretinoin [65].

8 Other Therapies

Zinc has been used in HS patients for its anti-inflammatory effects, and showed a positive response clinically. A retrospective study with 92 patients receiving 90 mg of zinc gluconate and 30 mg of nicotinamide reported the efficacy of oral zinc plus nicotinamide [66]. However, long-term pharmacologic doses of zinc compete with copper absorption and can cause anemia [67].

Although robust evidence is needed, there is one case report each for verapamil [68] and thalidomide [69], suggesting their potential efficacy.

9 Conclusions

The management of HS is complex and often requires a combination of medical and surgical treatments in order to achieve promising results for disease sufferers. Non-biologic and non-procedural treatments are often used as monotherapy for mild disease and can be used in conjunction with biologic therapy and surgery for moderate to severe disease. Recent studies highlighted in this review add support for the use of intralesional corticosteroids for HS flares and localized lesions, and there is evidence that monotherapy with tetracyclines may be as effective as the clindamycin/rifampicin combination. There is hope for the potential efficacy of add-on drugs to biologics to increase drug survival of the limited biologics available for HS.

HS treatment continues to remain a challenge and a refined understanding of disease pathogenesis will lead to more efficacious therapies in the armamentarium of therapeutic options. This review aims to assist clinicians in their decision making in the management of HS patients, which often requires multimodal, individualized approaches to address both the medical and psychiatric impacts of disease. With ongoing clinical trials with biologic and other immunomodulatory treatment options and stronger data supporting evidence-based guidelines, practicing dermatologists will have access to a greater variety of resources to support their HS patients that combine both medical and surgical approaches for optimal disease control.

Funding

No sources of funding were used to assist in the preparation of this manuscript.

References

1. Garg A, et al. Comorbidity screening in hidradenitis suppurativa: evidence-based recommendations from the US and Canadian Hidradenitis Suppurativa Foundation. J Am Acad Dermatol. 2021. 10.1016/j.jaad.2021.01.059 (Epub 23 Jan 2021).
2. Alavi A, Anooshirvani N, Kim WB, Coutts P, Sibbald RG. Quality-of-life impairment in patients with hidradenitis suppurativa: a Canadian study. Am J Clin Dermatol. 2015;16(1):61–5. [PubMed: 25432664]
3. Machado MO, et al. Depression and anxiety in adults with hidradenitis suppurativa: a systematic review and meta-analysis. JAMA Dermatol. 2019;155(8):939–45. [PubMed: 31166590]
4. Abdalla T, Lowes MA, Kaur N, Micheletti RG, Steinhart Ah, Alavi A. Is there a role for therapeutic drug monitoring in patients with hidradenitis suppurativa on tumor necrosis factor-alpha inhibitors. Am J Clin Dermatol. 2021;22(2):139–47. [PubMed: 33398848]
5. Flood KS, Porter ML, Kimball AB. Biologic treatment for hidradenitis suppurativa. Am J Clin Dermatol. 2019;20(5):625–38. 10.1007/s40257-019-00439-5. [PubMed: 31140067]
6. Garg A, et al. Evaluating patients' unmet needs in hidradenitis suppurativa: results from the Global Survey of Impact and Healthcare Needs (VOICE) Project. J Am Acad Dermatol. 2020;82(2):366–76. [PubMed: 31279015]
7. Zouboulis CC, et al. European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. J Eur Acad Dermatol Venereol. 2015;29:619–44. [PubMed: 25640693]
8. Danesh MJ, Kimball AB. Pyrithione zinc as a general management strategy for hidradenitis suppurativa. J Am Acad Dermatol. 2015;73(5):e175. [PubMed: 26475559]
9. Leiphart P, Ma H, Naik HB, Kirby JS. The effect of antimicrobial washes on antibacterial resistance in hidradenitis suppurativa. J Am Acad Dermatol. 2019;80(3):821–2. [PubMed: 30403961]
10. Alikhan A, et al. North American clinical management guidelines for hidradenitis suppurativa: a publication from the United States and Canadian Hidradenitis Suppurativa Foundations: Part II: Topical, intralesional, and systemic medical management. J Am Acad Dermatol. 2019;81(1):91–101. [PubMed: 30872149]
11. Leiphart P, Kitts S, Kirby JS. Adherence to over-the-counter antimicrobial washes in hidradenitis suppurativa patients. Dermatology. 2019;235(5):440–1. [PubMed: 31242490]
12. Fischer AH, Haskin A, Okoye GA. Patterns of antimicrobial resistance in lesions of hidradenitis suppurativa. J Am Acad Dermatol. 2017;76(2):309–13. [PubMed: 27742173]
13. Fisher S, Ziv M. Efficacy of topical ichthammol 10% for hidradenitis suppurativa: case series and systematic review of its use in dermatology. Dermatol Ther. 2020;33(6):e13868. [PubMed: 32558051]
14. Hunger RE, Laffitte E, Luchli S, et al. Swiss practice recommendations for the management of hidradenitis suppurativa/acne inversa. Dermatol. 2017;233:113–9.
15. Boer J, Jemec GBE. Resorcinol peels as a possible self-treatment of painful nodules in hidradenitis suppurativa. Clin Exp Dermatol. 2010;35(1):36–40. [PubMed: 19549239]
16. Molinelli E, et al. Efficacy and safety of topical resorcinol 15% as long-term treatment of mild-to-moderate hidratenitis suppurativa: a valid alternative to clindamycin in the panorama of antibiotic resistance. Br J Dermatol. 2020;183(6):1117–9. [PubMed: 32579711]
17. Docampo-Simón A, et al. Topical 15% resorcinol is associated with high treatment satisfaction in patients with mild to moderate hidradenitis suppurativa. Dermatology. 2021. 10.1159/000515450 (Epub 22 Apr 2021).
18. Riis PT, Boer J, Prens EP, et al. Intralesional triamcinolone for flares of hidradenitis suppurativa(HS): a case series. J Am Acad Dermatol. 2016;75:1151–5. [PubMed: 27692735]
19. Shanmugam VK, Zaman NM, McNish S, Hant FN. Review of current immunologic therapies for hidradenitis suppurativa. Int J Rheumatol. 2017;2017:8018192. [PubMed: 28912816]
20. Theut Riis P, Thorlacius LR, Jemec GB. Investigational drugs in clinical trials for hidradenitis suppurativa. Expert Opin Investig Drugs. 2018;27:43–53.

21. Fajgenbaum K, Crouse L, Dong L, Zeng D, Sayed C. Intralesional triamcinolone may not be beneficial for treating acute hidradenitis suppurativa lesions: a double-blind randomized, placebo controlled trial. Dermatol Surg. 2020;46(5):685–9. [PubMed: 31490300]
22. Fania L, et al. Intralesional ultrasound-guided combined treatment with triamcinolone plus lincomycin in hidradenitis suppurativa: a pilot study. Dermatol Ther. 2020;33(6):e13901. [PubMed: 32589335]
23. Caposiena Caro RD, Tartaglia C, Pensa C, Bianchi L. Intralesional therapy under ultrasound guidance in hidradenitis suppurativa: the importance of ultrasound evaluation. Dermatol Ther. 2020;33(6):e14116. [PubMed: 32737957]
24. Salvador-Rodriguez L, Arias-Santiago S, Molina-Leyva A. Ultrasound-assisted intralesional corticosteroid infiltrations for patients with hidradenitis suppurativa. Sci Rep. 2020;7(10):13363.
25. García-Martínez FJ, et al. Intralesional corticosteroid injection for the treatment of hidradenitis suppurativa: a multicenter retrospective clinical study. J Dermatolog Treatment. 2021;32(3):286–90.
26. Dautriche CN, et al. Tumescent triamcinolone infiltration: a new approach for the management of recalcitrant hidradenitis suppurativa. JAAD Case Rep. 2020;6(12):1310–2. [PubMed: 33294572]
27. Arenbergerova M, et al. Corticosteroid rescue therapy in relapsing hidradenitis suppurativa treated with adalimumab. J Eur Acad Dermatol Venereol. 2021;35(6):e381–3. [PubMed: 33539633]
28. Ingram JR, et al. Interventions for hidradenitis suppurativa. Cochrane Database Syst Rev. 2015. 10.1002/14651858.CD010081.pub2.
29. Ring HC, et al. The follicular skin microbiome in patients with hidradenitis suppurativa and healthy controls. JAMA Derm. 2017;153(9):897–905.
30. Kitts S, Govea R, Maczuga S, Kirby J. Long-term antibiotic use for the treatment of hidradenitis suppurativa consistent with guideline recommendations. Clin Exp Dermatol. 2021;46(3):582–3. [PubMed: 33202036]
31. Marasca C, et al. The pharmacology of antibiotic therapy in hidradenitis suppurativa. Expert Rev Clin Pharmacol. 2021;13(5):521–30.
32. Armyra K, Kouris A, Markantoni V, Katsambas A, Kontochristopoulos G. Hidradenitis suppurativa treated with tetracycline in combination with colchicine: a prospective series of 20 patients. Int J Dermatol. 2017;56(3):346–50. [PubMed: 28054351]
33. Jorgensen AHR, Yao Y, Thomsen SF, Ring HS. Treatment of hidradenitis suppurativa with tetracycline, doxycycline, or lymecycline: a prospective study. Int J Dermatol. 2021;60(7):785–91. 10.1111/ijd.15459. [PubMed: 33660281]
34. van der Zee HH, Boer J, Prens EP, Jemec GBE. The effect of combined treatment with oral clindamycin and oral rifampicin in patients with hidradenitis suppurativa. DermatologyTet. 2009;219(2):143–7.
35. Pradhan S, Madke B, Kabra P, Singh AL. Anti-inflammatory and immunomodulatory effects of antibiotics and their use in dermatology. Indian J Dermatol. 2016;61(5):469–81. [PubMed: 27688434]
36. Robert E, et al. Non-surgical treatments for hidradenitis suppurativa: a systematic review. Ann Chir Plast Esthet. 2017;62(4):274–94. [PubMed: 28457725]
37. Yao Y, Jørgensen AR, Ring HC, Thomsen SF. Effectiveness of clindamycin and rifampicin combination therapy in hidradenitis suppurativa: a 6-month prospective study. Br J Dermatol. 2021;184(3):552–3. [PubMed: 33000461]
38. Bettoli V, Toni G, Odorici G, Forconi R, Corazza M. Oral clindamycin and rifampicin the treatment of hidradenitis suppurativa-acne inversa in patients of pediatric age: a pilot prospective study. Br J Dermatol. 2021;185(1):216–7. 10.1111/bjd.19867. [PubMed: 33544882]
39. van Straalen KR, et al. 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. 2021;85(2):369–78. 10.1016/j.jaad.2020.12.089. [PubMed: 33484766]
40. Caposiena Caro RD, Molinelli E, Brisigotti V, Offidani A, Bianchi L. Lymecycline vs. clindamycin plus rifampicin in hidradenitis suppurativa treatment: clinical and ultrasonography evaluation. Clin Exp Dermatol. 2021;46(1):96–102. [PubMed: 32683727]

41. Caposiena Caro RD, et al. Clindamycin versus clindamycin plus rifampicin in hidradenitis suppurativa treatment: clinical and ultrasound observations. J Am Acad Dermatol. 2019;80(5):1314–21. [PubMed: 30502416]
42. Rosi E, et al. Clindamycin as unique antibiotic choice in hidradenitis suppurativa. Dermatol Ther. 2019;32(2):e12792. [PubMed: 30515931]
43. Deshpande A, et al. Community-associated Clostridium difficile infection and antibiotics: a meta-analysis. J Antimicrob Chemother. 2013;68(9):1951–61. [PubMed: 23620467]
44. Delage M, et al. Rifampin-moxifloxacin-metronidazole combination therapy for severe Hurley Stage 1 hidradenitis suppurativa: prospective short-term trial and one-year follow-up in 28 consecutive patients. J Am Acad Dermatol. 2020. 10.1016/j.jaad.2020.01.007 (Epub 10 Jan 2020).
45. Ring HC, Knudsen A, Thomsen SF. Metronidazole for hidradenitis suppurativa: future potential treatment applications. J Eur Acad Dermatol Venereol. 2021;35(5):e323–4. [PubMed: 33393693]
46. Graham DR, et al. Ertapenem once daily versus piperacillin-tazobactam 4 times per day for treatment of complicated skin and skin-structure infections in adults: results of a prospective, randomized, double-blind multicenter study. Clin Infect Dis. 2002;34:1460–8. [PubMed: 12015692]
47. Join-Lambert O, et al. Efficacy of ertapenem in severe hidradenitis suppurativa: a pilot study in a cohort of 30 consecutive patients. J Antimicrob Chemother. 2016;71(2):513–20. [PubMed: 26565016]
48. Lyons AB, Parks-Miller A, Zubair R, Hamzavi IH. Ertapenem—a potent treatment for clinical and quality of life improvement in patients with hidradenitis suppurative—reply. Int J Dermatol. 2019;58(4):E88. [PubMed: 30515760]
49. Yazdanyar S, Boer J, Ingvarsson G, Szepietowski JC, Jemec GB. Dapsone therapy for hidradenitis suppurativa: a series of 24 patients. Dermatology. 2011;222(5):342–6. [PubMed: 21757878]
50. Murray G, Hollywood A, Kirby B, Hughes R. Dapsone therapy for hidradenitis suppurativa. Br J Dermatol. 2020;183(4):767–8. [PubMed: 32294243]
51. Riis PT, Ring HC, Themstrup L, Jemec GB. The role of androgens and estrogens in hidradenitis suppurative—a systematic review. Acta Dermatovenerol Croat. 2016;24(4):239–49. [PubMed: 28128074]
52. Vossen AR, van Straalen KR, Prens EP, van der Zee HH. Menses and pregnancy affect symptoms in hidradenitis suppurativa: a cross-sectional study. J Am Acad Dermatol. 2017;76(1):155–6. [PubMed: 27986138]
53. Mortimer PS, Dawber RP, Gales MA, Moore RA. A double-blind controlled cross-over trial of cyproterone acetate in females with hidradenitis suppurativa. Br J Dermatol. 1986;115(3):263–8. [PubMed: 2944534]
54. Karagiannidis I, Nikolakis G, Sabat R, Zouboulis CC. Hidradenitis suppurativa/acne inversa: an endocrine skin disorder? Rev Endocr Metab Disord. 2016;17(3):335–41. [PubMed: 27294593]
55. Golbari NM, Porter ML, Kimball AB. Antiandrogen therapy with spironolactone for the treatment of hidradenitis suppurativa. J Am Acad Dermatol. 2019;80(1):114–9. [PubMed: 30003993]
56. Quinlan C, Kirby B, Hughes R. Spironolactone therapy for hidradenitis suppurativa. Clin Exp Dermatol. 2020;45(4):464–5. [PubMed: 31602704]
57. Jennings L, Hambly R, Hughes R, Moriarty B, Kirby B. Metformin use in hidradenitis suppurativa. J Dermatol Treat. 2020;31(3):261–4.
58. Kraft JN, Searles GE. Hidradenitis suppurativa in 64 female patients: retrospective study comparing oral antibiotics and antiandrogen therapy. J Cutan Med Surg. 2007;11(4):125–31. [PubMed: 17601419]
59. Moussa C, Wadowski L, Price H, Mirea L, O'Haver J. Metforin as adjunctive therapy for pediatric patients with hidradenitis suppurativa. J Drugs Deramtol. 2020;19(12):1231–4.
60. Alikhan A, Lynch PJ, Eisen DB. Hidradenitis suppurativa: a comprehensive review. J Am Acad Dermatol. 2009;60(4):539–61. [PubMed: 19293006]
61. van Straalen KR, Schneider-Burrus S, Prens EP. Current and future treatment of hidradenitis suppurativa. Br J Dermatol. 2020;183(6):e178–87. [PubMed: 29981245]
62. Patel N, et al. Isotretinoin in the treatment of hidradenitis suppurativa: a retrospective study. J Dermatol Treat. 2021;32(4):473–5.

63. McPhie ML, Bridgman AC, Kirchhof MG. Combination therapies for hidradenitis suppurativa: a retrospective chart review of 31 patients. J Cutan Med Surg. 2019;23(3):270–6. [PubMed: 30658534]

64. Pilkington T, Brogden RN. Acitretin: a review of its pharmacology and therapeutic use. Drugs. 1992;43:597–627.

65. Scheman AJ. Nodulocystic acne and hidradenitis suppurativa treated with acitretin: a case report. Cutis. 2002;69(4):287–8. [PubMed: 12080949]

66. Dhaliwal S, et al. Effects of zinc supplementation on inflammatory skin diseases: a systematic review of clinical evidence. Am J Clin Dermatol. 2020;21(1):21–39. [PubMed: 31745908]

67. Molinelli E, et al. Efficacy of oral zinc and nicotinamide as maintenance therapy for mild/moderate hidradenitis suppurativa: a controlled retrospective clinical study. J Am Acad Dermatol. 2020;83(2):665–7. [PubMed: 32339699]

68. Laroche ML, Teste M, Vanoost J, Geniaux H. Successful control of hidradenitis suppurativa with verapamil: a case report. Fundam Clin Pharmacol. 2019;33(1):122–4. [PubMed: 30025186]

69. Hotz C, Sbidian E, Oro SIH, Chosidow O, Wolkensein P. Thalidomide in severe hidradenitis suppurativa: a therapeutic option. Acta Derm Venereol. 2019;99(12):1170–1. [PubMed: 31314122]

Key Points

Recent studies add support for the use of intralesional corticosteroids for hidradenitis suppurativa (HS) flares and localized lesions.

A recent study suggests that monotherapy with tetracyclines may be as effective as the clindamycin/rifampicin combination.

Non-biologic drugs may be useful adjuncts to the biologic therapy of HS.

Table 1

Recent studies of non-biologic medical treatments for hidradenitis suppurativa (2019–2021)

Treatment	Sample size (*N*)	LOE (type of study)[a]	Key message	First author (year)
Topical therapy				
Topical ichthammol 10% twice daily for 10 days	20	4 (case-series study)	Decreased abscess size with no adverse effects	Fisher (2020) [13]
Topical resorcinol 15% cream once daily for 12 weeks	61	4 (interventional prospective study)	Decrease in IHS4 at 4 weeks ($p < 0.001$) and 12 weeks ($p < 0.05$)	Molinelli (2020) [16]
Topical 15% resorcinol	92	4 (cross-sectional study)	15% of patients were satisfied and 84.8% would recommend the treatment	Docampo- Simón (2021) [17]
Intralesional and systemic steroids				
Intralesional triamcinolone 10 mg/mL, 40 mg/mL, and normal saline over a 14-day period	32	2 (double-blind, randomized, placebo-controlled trial)	No significant difference in days to HS inflammatory lesion clearance, pain reduction at day 5, or patient satisfaction	Fajgenbaum (2020) [21]
Intralesional ultrasound-guided combined treatment with triamcinolone 40 mg plus lincomycin 600 mg	36	4 (interventional prospective study)	Decrease in mean VAS values for pain ($p = 0.027$) Bodily Pain scale of the Short-Form Health Survey (SF-36) improved at 4 weeks ($p < 0.001$)	Fania (2020) [22]
Two injections at baseline and after 2 weeks				
Intralesional triamcinolone 40 mg/mL and lincomycin 300 mg/mL therapy under ultrasound guidance	8	4 (interventional prospective study)	Treatment combination shows statistically significant reduction of HS symptoms and pain	Caposiena Caro (2020) [23]
Two injections at baseline and after 4 weeks				
Intralesional ultrasound-guided triamcinolone 40 mg/mL once weekly for 12 weeks	77	2 (interventional prospective study)	Decrease in IHS4 at 12 weeks ($p < 0.001$) Hurley stage negatively correlated with complete response for abscesses and draining fistulas at – 0.17 ($p < 0.01$) and −0.30 ($p < 0.02$)	Salvador- Rodriguez (2020) [24]
Intralesional corticosteroid injection (the most common corticosteroid applied was triamcinolone; dosage was between 0.5 and 1 mL)	98	4 (observational, retrospective study)	Complete response in 70.4% of lesions, partial response in 25.2% of lesions, no response in 4.4% of lesions Improved response rates if previously evaluated with ultrasound	García-Martínez (2021) [25]
Tumescent triamcinolone infiltration 250 mL of saline, 25 mL of 1% lidocaine with epinephrine, and 120 mg of triamcinolone in the form of a 40 mg/mL solution delivered once	1	5 (case report)	Efficacy of tumescent triamcinolone injection for the treatment of aggressive/recalcitrant HS in the setting of Crohn's disease	Dautriche (2020) [26]
Intralesional methylprednisolone versus oral prednisone in patients treated with adalimumab 1. Methylprednisolone 40 mg injection twice in 2-week intervals 2. Oral prednisone 10 mg daily for 8–12 weeks	38	2 (interventional prospective study)	Efficacy of intralesional or low-dose systemic prednisone in combination with adalimumab in relapsing HS in improving IHS4 DLQI and pain	Arenbergerova (2021) [27]
Antibiotic therapy				
Tetracyclines: Oral tetracycline 500mg twice daily, doxycycline 100 mg twice daily, lymecycline 300 mg twice daily for 4 months	108	2 (prospective study)	Improvement in HSS at follow-up ($p < 0.0001$)	Jorgensen (2021) [33]

Treatment	Sample size (*N*)	LOE (type of study)[a]	Key message	First author (year)
Combination therapy with clindamycin 300 mg and rifampicin 300 mg twice daily for 6 months	54	4 (open-label, single-group, prospective study)	Improvement in HSS ($p < 0.001$)	Yao (2021) [37]
Combination therapy with oral clindamycin (600 mg daily) and rifampicin (600 mg daily) for 10 weeks	20 (aged ≥16 years)	4 (pilot prospective study)	Reduction in Sartorius score and number of exacerbations after treatment ($p = 0.001$)	Bettoli (2021) [38]
Tetracyclines and clindamycin plus rifampicin: Oral tetracyclines (tetracycline 500 mg twice daily, doxycycline 100 mg once daily, minocycline 100 mg once daily) or clindamycin 300 mg twice daily with rifampicin 600 mg once daily for 12 weeks	283	2 (prospective cohort study)	Decrease in IHS4 in the tetracycline group ($p < 0.001$) and the clindamycin and rifampicin combination group ($p < 0.001$)	van Straalen (2021) [39]
Tetracycline (lymecycline 300 mg daily) versus combination therapy clindamycin and rifampicin (600 mg plus 600 mg daily) for 10 weeks	52	3 (retrospective study)	Improvement in IHS4, VAS, and DLQI baseline ($p < 0.001$), particularly in the tetracycline group	Caposiena Caro (2021) [40]
Clindamycin 150 mg four times daily versus clindamycin 150 mg four times daily plus rifampicin 300 mg twice daily for 8 weeks	60	3 (retrospective comparative study)	Improvement in IHS4 score, DLQI ($p = 0.037$) and VAS ($p = 0.038$), particularly in the clindamycin monotherapy group Reductions in nodule and abscess counts were similar between the groups Marked decrease in the number of draining tunnels in the clindamycin monotherapy group ($p = 0.002$)	Caposiena Caro (2019) [41]
Clindamycin 300 mg twice daily for 12 weeks	31	4 (retrospective study)	Reduction in disease severity parameters ($p < 0.01$)	Rosi (2019) [42]
Oral combination of rifampin (10 mg/kg once daily), moxifloxacin (400 mg once daily), and metronidazole (250– 500 mg three times daily) [RMoM] treatment	28 (19 patients were treated for 6 weeks by RMoM, followed by 4 weeks of RMo alone, then by cotrimoxazole after remission)	4 (prospective, open-label, non-comparative cohort study)	Reduction in Sartorius score at 12 weeks ($p = 6 \times 10^{-6}$) 75% of patients reaching clinical remission ($p = 0.049$) Decrease in the number of flares per year flares ($p = 10^{-5}$)	Delage (2020) [44]
Dapsone 50–200 mg/day (mostly 100 mg/day) for 2 weeks-7 months	24	4 (case series)	Improvement was seen in 9 of 24 (38%) treated patients, whereas 15 of 24 (62%) did not experience any improvement. Rapid recurrence after treatment cessation is a concern	Yazdanyar (2011) [49]
Dapsone 50 mg once daily titrated up according to response and tolerability: 18 patients (72%) received 100 mg, one patient (4%) received 150 mg, and one patient (4%) received 200 mg; 5 patients (20%) remained on 50 mg	25	4 (retrospective review study)	Subjective clinical improvement was seen in 16 (64%) patients. Dapsone appears to be an effective and well-tolerated treatment option for HS in patients with Hurley stage I and II disease	Murray (2020) [50]
Hormonal therapies				
Spironolactone 75 mg once daily over a 7-month period	67	4 (single-center chart retrospective review)	Patients achieved significant disease improvement with regard to pain (Δ – 1.5; $p = 0.01$), inflammatory lesions (Δ – 1.3; $p = 0.02$), and HS-PGA score (Δ – 0.6; $p < 0.001$). No change was found for Hurley stage and fistulas. There was no difference in improvement between subjects who received < 75 mg of spironolactone and those who received > 100 mg daily	Golbari (2019) [55]
Spironolactone 100 mg ($n = 22$) or 50 mg ($n = 4$) daily Mean 6 months (range 2–17 months)	26	4 (retrospective chart review)	Spironolactone was effective in 35% of patients, with a reduction in DLQI of > 5	Quinlan (2020) [56]

Treatment	Sample size (*N*)	LOE (type of study)[a]	Key message	First author (year)
Metformin (mean dose 1.5 g once daily over a mean period of 11 months)	53	4 (retrospective chart review)	Subjective clinical response was seen in 68% of patients, with 19% of these having quiescent disease with metformin monotherapy. 25% had no improvement Gastrointestinal adverse effects in 11% of patients	Jennings (2020) [57]
Metformin	16	4 (retrospective chart review)	For some pediatric patients, metformin as an adjunctive therapy may help improve the control of HS with minimal adverse effects	Moussa (2020) [59]
Retinoids				
Isotretinoin	209	4 (retrospective chart review)	Demonstrates a 35.9% response rate based on patients' outcome assessment, while 64.1% of patients reported no response. When comparing responders with non-responders, responders were more likely to have a history of pilonidal cyst ($p = 0.024$).	Patel (2021) [62]
Various combination therapies	31	4 (retrospective chart review)	Suggests that combination therapy with isotretinoin/spironolactone for mild disease, isotretinoin or doxycycline with adalimumab for moderate disease, and cyclosporine/adalimumab for severe disease appears to be an effective method of HS management, however no statistical results are provided	McPhie (2019) [63]
Others				
Oral therapy with capsules containing 90 mg of zinc gluconate and 30 mg of nicotinamide once daily for 90 days	92	3 (controlled retrospective clinical study)	Demonstrate a significant reduction in the number and mean duration of acute flares in the treated versus control groups. Patients in the treated group correspondingly reported a marked reduction in mean VAS, DLQI, and IHS4 scores compared with the control group at both 12 and 24 weeks ($p < 0.005$)	Molinelli (2020) [67]
Verapamil 240 mg three times daily for 2 months	1	5 (case report)	When verapamil was stopped, the lesions recurred within 1.5 months. The patient resumed taking verapamil before and after remission occurred	Laroche (2019) [68]
Thalidomide 50 mg daily for 2 months then 100 mg daily for 4 months	6	5 (case report)	Demonstrates the potential efficacy of daily treatment with thalidomide 100 mg for 4 months in patients with severe inflammatory HS showing failure of conventional treatments based on recent published guidelines	Hotz (2019) [69]

LOE level of evidence, *IHS4* International Hidradenitis Suppurativa Severity Score System, *HS* hidradenitis suppurativa, *VAS* visual analog scale, *DLQI* Dermatology Life Quality Index, *HSS* Hidradenitis Suppurativa Score, *PGA* Physician Global Assessment

[a]1 = randomized controlled trial; 2 = prospective cohort study; 3 = case-control study, retrospective cohort study; 4 = case series, uncontrolled cohort study; 5 = expert opinions, case report