Scientific evidence for the use of current traditional systemic therapies in patients with hidradenitis suppurativa

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Traditional systemic therapies are frequently prescribed for the treatment of hidradenitis suppurativa (HS). Clinicians consider antibiotics, retinoids, antiandrogens, immunosuppressants, and less common treatment, such as fumarates, in the management of HS. Different classes of medications have been selected to treat HS based on their ability to target various pathways of the condition. Concerns about infection, such as infection with *Clostridium difficile*, necessitates switching therapy or shortening the course of therapy with specific antibiotics. This review explores the outcomes with the use of numerous medical therapies and postulates explanations for their efficacy or lack of response. Data on long-term safety and efficacy with traditional systemic therapies are lacking. (J Am Acad Dermatol 2015;73:S42-6.)

Key words: antiandrogens; antibacterials; evidence-based medicine; fumarates; hidradenitis suppurativa; immunosuppressants; retinoids; zinc.

INTRODUCTION

Systemic therapies are the mainstay of treatment for patients with hidradenitis suppurativa (HS). Patients with HS are prescribed on average 1.6 treatments per visit.[1] Physicians are faced with the challenge of selecting the most effective therapies given the limited evidence with respect to the use of specific medications.[2] In this article, we review evidence for the use of traditional systemic therapies in patients with HS (Fig 1).

ANTIBIOTICS

Systemic antibiotics are the medications most often prescribed to treat HS, and as a group, these agents have been shown to be the most effective traditional systemic therapy.[1,2] In a recent survey of physicians in the United Kingdom, tetracyclines were the most frequently prescribed first-line oral therapy for HS, and a combination of rifampin and clindamycin was the first choice for second-line oral therapy.[3]

It is likely that the efficacy of antibiotics against HS is related in part to their anti-inflammatory properties. Tetracyclines have been shown to suppress lymphocytes, neutrophils, and histiocytes, all of which are present in HS lesions.[4-6] Similarly, rifampin, ciprofloxacin, and ampicillin exert negative immunomodulatory effects.[7] Matusiak et al[8] recently suggested that the selection of antibiotics for the treatment of HS should be based on the efficacy of those agents against specific bacterial isolates extracted from HS lesions. The authors found that carbapenems, penicillins with β-lactamase inhibitors, and fluoroquinolones were most effective against such isolates, a finding that implicates bacterial biofilm in the pathophysiology of HS.[8] However, the biofilm hypothesis is contradicted by the efficacy of immunosuppressive therapies. In our opinion, it is more likely that bacterial biofilm is secondary to the initial follicular occlusion and the subsequent inflammatory response.

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Rifampin and clindamycin

The efficacy of a combination of rifampin and clindamycin in the treatment of HS was documented in several modestly large case series (total number of patients, 141).[9-12] The treatment course in the majority of studies consisted of a combination of rifampin 600 mg and clindamycin 600 mg administered in a single dose or in 2 divided daily doses for 10 consecutive weeks. Although the definition of "response" varied among studies, an average of 81% (range, 71-85%) of the subjects had some response to therapy. However, treatment with clindamycin is a major risk factor for the development of infection with *Clostridium difficile*, and the extensive list of possible drug interactions with rifampin further limits the use of the combination of rifampin and clindamycin in the treatment of HS.

CAPSULE SUMMARY

- Systemic antibiotics have the best evidence among oral therapies for treating hidradenitis suppurativa.
- Long-term efficacy and safety data are limited or nonexistent for traditional systemic therapies.
- While traditional systemic therapies may be first-line modalities for the treatment of hidradenitis suppurativa, there is no single first-line choice.

Antibiotic use is the strongest risk factor for community-acquired *C difficile* infection (CA-CDI), and clindamycin poses the highest relative risk for the development of that disease (odds ratio, 20.43 [95% confidence interval, 8.50-49.09]).[13,14] In a population-based study in which the incidence of CA-CDI was 6.9 cases per 100,000 people, 19% of the patients with that disease had been recently treated with clindamycin, which poses a risk second only to that associated with fluoroquinolone therapy.[15] Because the risk of *C difficile* infection is positively correlated with the duration of antibiotic therapy, it has been recommended to alternate combination rifampin and clindamycin treatment with other treatments.[16]

Because of its induction of the cytochrome P450 pathways, rifampin is associated with a lengthy list of drug interactions,[17] and its interaction with hypoglycemic drugs and oral contraceptives is especially relevant in the HS population. Interestingly, an interaction between rifampin and clindamycin that resulted in an 82% to 93% reduction in clindamycin peak/trough blood levels has been shown, but the clinical significance of that finding is unclear.[18]

Tetracycline

Tetracycline is the only traditional systemic antibiotic that has been examined in a randomized controlled study in the treatment of HS. Jemec and Windelboe[19] randomized 46 patients with mild to moderate HS to receive topical clindamycin 1% twice daily or oral tetracycline 500 mg twice daily. Patients in both groups had significant improvement from baseline after 3 months of treatment, as revealed by both patient and Physician Global Assessment. There was no statistically significant difference between the results of treatment for HS with topical clindamycin as opposed to oral tetracycline, but given its relatively small sample size and significant dropout rate, that study was likely underpowered to detect any difference.[2]

Doxycycline is also frequently used to treat HS because it can be taken with food.[8] Few reports on the use of minocycline in the treatment of HS have been published, probably because minocycline is associated with a higher risk of hypersensitivity syndrome and drug-induced lupus.[20] Because 64% of the bacteria isolated from HS lesions are resistant to tetracyclines, it is likely that those agents exert an anti-inflammatory effect.[8]

Dapsone

Dapsone is a sulfone antibiotic that in addition to its antimicrobial effect suppresses both neutrophil and eosinophil peroxidase enzymes; therefore, it is frequently used to treat neutrophilic and eosinophilic inflammatory dermatoses.[21] The use of dapsone for the treatment of HS has been described in several reports.[22-24] In a study of 24 patients with HS, 25% achieved significant improvement and 12.5% experienced slight improvement in their disease after treatment with dapsone.[24] If patients treated with dapsone are monitored appropriately, it is relatively safe, and we have found dapsone to be useful as long-term maintenance therapy for individuals with HS.

Other antibiotic treatments for HS

A study by Join-Lambert et al[25] found that 57% of 28 patients treated with a combination of rifampin, moxifloxacin, and metronidazole achieved complete clearance of their HS lesions. Those positive results might be inflated, however, because half of the patients studied also received 2 weeks of intravenously administered ceftriaxone as induction therapy.

The long-term use of moxifloxacin, which is a fluoroquinolone, is a potential concern because of the increased risk of both tendonitis and *C difficile* infection.[15,26]