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Review Article

Complementary and Alternative Treatments for Hidradenitis Suppurativa: A Systematic Review

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Hidradenitis Suppurativa (HS) is a chronic inflammatory disease characterized by recurrent painful and deep dermal abscesses, sinus tracts, and dermal contractures. HS significantly reduces quality of life and leads to long-term sequelae impacting physical and mental well-being. Despite conventional therapies such as antibiotics and immunomodulators, management remains challenging and marked by recurrences, undesirable side effects, and financial burden. Faced with such choices, many patients seek complementary and alternative medicine modalities (CAMs). Literature on CAMs for HS is sparse and deficient in evidence-based clinical data. Several reviews cover non-pharmacological approaches to HS, however we aim to include CAMs such as Ayurveda and Traditional Chinese Medicine (TCM).

A literature search was conducted utilizing PRISMA guidelines in 8 databases on complementary and alternative therapies in HS over the last decade. No randomized controlled trials were found. However, a combination of 42 systematic reviews, retrospective and prospective studies, case series and reports were included in this review article. Results on CAMs for HS yielded a higher frequency of literature and evidence supporting lifestyle changes such as smoking cessation, weight loss and dietary modifications. Other treatments that have shown some positive clinical effects include zinc, vitamin D, curcumin, TCM, Ayurveda, wound care dressings for HS lesions, and mental health management. There is currently not enough evidence to recommend the use of these CAMs for HS, but the current data is promising for future investigations and large-scale clinical trials.

1. INTRODUCTION

Hidradenitis suppurativa (HS), also known as acne inversa or Verneuil's disease, is a chronic, debilitating inflammatory disease of the follicular epithelium.[1,2] HS has an estimated prevalence ranging from 0.05% to 4%, with a higher incidence of disease among females, African Americans, and biracial individuals.[3-5] Clinically, the disease presents with tender subcutaneous nodules primarily involving the axillae, perineum, and inframammary regions.[1] The lesions rupture and coalesce to form painful deep dermal abscesses with sinus tracts, and eventual fibrosis and dermal contractures post-healing.[1] Although not well understood, there has been a shift in the understanding of the pathogenesis from a disorder of apocrine origin to a predominance of follicular occlusion as the primary etiology.[6] Bacteria mostly exacerbate disease and are not primary etiologic agents.[1] Further, recent studies have shown that genetic susceptibility and immune dysregulation play a key role in propagating the inflammatory cascade, primarily tumor necrosis factor-alpha (TNF-α) and interleukin-17 (IL-17).[7]

HS significantly decreases quality of life (QOL) and is associated with several psychological and emotional consequences, social and work impairment, and significant pain.[3] Current management for HS is primarily through medical and surgical means and often determined by Hurley staging of disease, pain, and QOL measurements. The Hurley system is a widely used classification tool to determine severity of disease, categorizing involvement into three stages utilizing quantity of nodules and abscesses, sinus tract formation, and extent of scarring.[8] Current evidence on HS management include a combination of treatments ranging from topical/intralesional therapies, systemic antibiotics, hormonal therapies, retinoids, systemic immunomodulators, and biologics.[9] Despite the numerous conventional medical and surgical options for HS, concerns about side ef-

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fects, financial burden, and appropriate management of comorbidities persist.

There is a need for effective treatment with fewer undesirable side effects, specifically in this cohort of patients requiring long-term management. Identifying innovative ways to reduce the burden of a chronic disease course requires further research into the safety and efficacy of treatments, including those outside of the conventional practice. Equally important, accessibility of health care and adequate resources may be another impedance in receiving appropriate treatment. Studies have found that a low socioeconomic status (SES) has been associated with a higher risk of disease, and that up to 25% of patients with HS are unemployed, with an additional 9.4% are on leave due to disability.[10-12] Given these factors, an increase in provider awareness of alternative methods to managing HS, such as a reduction in smoking or dietary modifications, may benefit individuals who are not able to access further means of management. Accessible and effective options for management are highly desirable, considering the disproportionate numbers of HS patients with low SES or unemployment.

While the utilization of complementary and alternative medicine modalities (CAMs) is sought by many individuals with chronic inflammatory conditions such as HS, strong evidence their use is limited. In a large survey by Price *et al.* examining the use of CAMs in HS, nearly half of the respondents perceived conventional therapy as not very successful, and 84.2% of respondents reported using CAMs.[13] Only 69.4% reported informing a health care provider about their use of CAMs,[14] suggesting low transparency with providers and conversely, minimal inquiries on their use from a clinician standpoint. Evidence-based therapeutic benefits and limitations for CAMs are lacking in literature, making it challenging for clinicians to appropriately recommend alternative treatments. To date, there are no published randomized controlled trials (RCTs) examining the use of CAMs in HS. While sufficient clinical data is lacking, this review aims to systematically review the current literature and compile a brief overview of the use and role of CAMs in the management of HS.

2. METHODS

A systematic review was performed using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. The primary research question being assessed is as follows: In patients with Hidradenitis Suppurativa, what are the potential roles, if any, of various CAM modalities in the management of HS symptomatology or disease outcomes? We aim to review the modalities discussed in the literature and we hypothesize that CAMs may play a positive role in HS management, warranting further research into these interventions.

2.1. ELIGIBILITY CRITERIA

Literature analyzed in this review are mostly observational and qualitative, due to the lack of controlled clinical trials in the realm of alternative treatments for HS. Study types included systematic reviews, cohort studies, narrative review papers, case series, case reports, survey data, and expert opinion articles. The contents of each article were manually reviewed, and the article was subsequently included if the following criteria were met: (1) published in English; (2) discussed HS as the primary disease process; (3) studied any form of management considered a complementary or alternative method of treatment; (4) CAM intervention was utilized without prior to- or post-conventional medical or surgical management. Exclusion criteria were as follows: (1) primary intervention discussed was medical management of HS with pharmaceutical, surgical, or other procedural treatment as these articles are out of scope for the aim of this review; (2) conventional medical intervention was studied during course of treatment with CAM modality; (3) full text of article not available. No limits were placed on number of subjects or study design.

2.2. INFORMATION SOURCES AND SEARCH STRATEGY

The search strategy utilized a computerized search of a total of 8 databases including PubMed, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, Alt HealthWatch, Global Health, International Pharmaceutical Abstracts and Academic Search Premier databases. Additionally, Google Scholar was used to derive relevant articles specifically related to Ayurveda, Traditional Chinese Medicine (TCM) and acupuncture that were referenced in other studies. The search included all articles published from 2011 onwards to review the most recent literature over the last decade. The search included all articles published on or before October 2, 2021. Search strategies were created by one author following consultation with an academic librarian. The following Medical Subject Heading (MeSH) terms were used: (hidradenitis suppurativa, acne inversa, Verneuil's disease) and (complementary, alternative, integrative, traditional, homeopathic, natural, ayurvedic, acupuncture, weight, acupressure, massage, compress, zinc, turmeric, curcumin, vitamin, supplement, pyridoxine, cobalamin, herb, herbal, oil, honey, brewer's yeast, smoking, balneotherapy, hydrotherapy, cryotherapy, aromatherapy, meditation, hypnosis, biofeedback, phytotherapy,) and (treatment, medicine, therapy, therapies, management). Literature search results were exported and subsequently organized through EndNote, a Clavirate® reference management software.

2.3. STUDY SELECTION

One author (AB) screened the titles and abstracts of studies to remove duplicates and for inclusion based on predetermined criteria. Both authors (AB and PL) independently assessed the full texts of the selected studies that met eligibility criteria in an unblinded manner. 43 total articles were determined to be eligible for inclusion in the systematic review (Fig. 1).

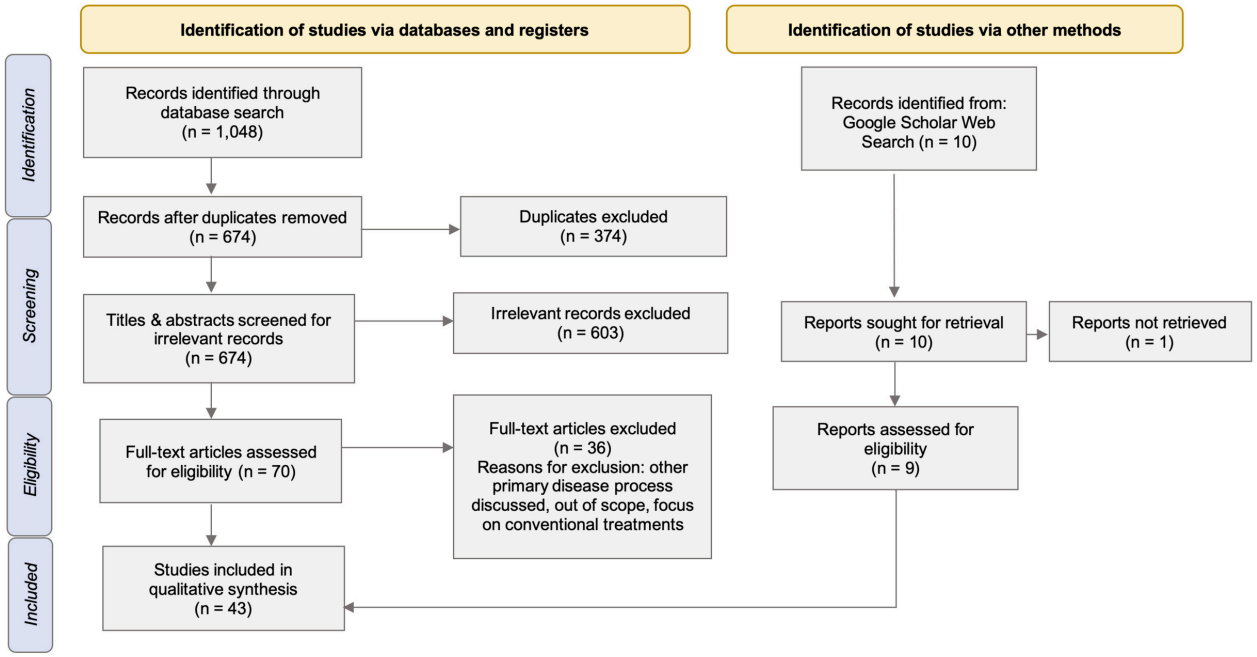

Fig. I – PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram detailing the study selection process and number of studies obtained through the systematic search, screening, eligibility, and inclusion stages.*

*Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

2.4. DATA EXTRACTION

Both authors (AB and PL) extracted data from the selected studies and organized them by intervention. Studies were categorized, based on primary intervention discussed, into the following groups: lifestyle modifications; dietary alterations; vitamins, minerals, and supplements; Traditional Chinese Medicine (TCM); Ayurveda; wound care; and mental health management. Authors extracted data on intervention, study design, efficacy of intervention and outcomes for HS, individual study limitations, and quality of evidence. No specific criteria were determined for efficacy of intervention and authors extracted data on any outcome playing a role in HS symptomatology or course of disease (improvement in pain, number of abscesses, symptom regression, inflammation etc.). This included both subjective and objective measurements.

2.5. OUTCOMES

The primary outcomes assessed were improvements in HS severity, symptomatology, or disease outcomes through CAM modalities. Markers of improvement included any measure of disease course, or effect on HS, including patient self-reported disease improvement. Improvements in quality of life or severity scales for HS that were utilized by studies, were also recognized as markers of improvement for this review.

2.6. RISK OF BIAS ACROSS STUDIES

Studies were assessed for quality utilizing the Scottish Intercollegiate Guidelines Network (SIGN) grades for evidence.[15] Evaluation of study quality utilizing this grading system assesses for type of study, bias among studies and probability of causal relationships. One author (AB) utilized these criteria for grading the studies and uncertainties were resolved by consultation with second author (PL).

2.7. DATA SYNTHESIS

Due to the variability in anticipated clinical data and study types included, this review is a qualitative synthesis.

3. RESULTS

Our literature search yielded 1,058 results, of which, 43 studies were included in the final review. Summary of qualitative data synthesis is presented in Table 1, which lists each study analyzed that yielded recordable outcomes or recommendations (n = 32). The remainder (n = 11) were utilized throughout the review as supporting evidence. The results are categorized by CAM modality and discussed below.

3.1. SMOKING CESSATION AND WEIGHT LOSS

Smoking cessation and weight loss are the crux of lifestyle modification in HS. Studies have shown that tobacco smoke as well as nicotine products promote proinflammatory cy-

Table 1. Summary Table of Alternative Treatments for HS

Treatment Modality	Intervention	Year, Study, Country	Study Design	Recommendations	Study Limitations	Quality of Evidence*
Lifestyle modification	Smoking cessation	2020, Acharya et al.,[15] Nepal	Meta-Analysis	• Screen patients for active smoking status due to high incidence in HS & smoking associated morbidity	Inability to provide a causal relationship between smoking and HS; inability to provide evidence of direct relationship between smoking cessation and improvement of HS	1-
		2019, Cheng et al.,[16] Singapore	Retrospective Study	• Structured pharmacy-led smoking cessation clinics can be effective at reducing smoking in HS patients	Inability to provide evidence of direct correlation between smoking cessation and improvement of HS	2-
	Weight loss	2016, Boer J.,[17] England	Case Report	• Weight reduction may improve areas of friction and decrease overall inflammation	Significant weight reduction (>30kg) and study was limited to one case	3
Diets	Brewer's & Baker's Yeast	2013, Cannistrà,[18] France & Italy	Prospective Study	• Yeast exclusion diet after medical/ surgical management • If indicated by positive serology for anti-*saccharomyces cerevisiae* antibodies: discontinuation of foods such as beer, wine, breads & baked products	Small sample size; Patients underwent surgery before yeast exclusion diet	2-
		2020, Aboud et al.,[19] France	Prospective Study	• Yeast exclusion diet prior to medical/surgical treatment • If indicated by positive serology for anti-*saccharomyces cerevisiae* antibodies: discontinuation of bakery products, vinegar, black tea, soy sauces, beer, wine, fermented cheeses, and mushrooms	Self-reported control of flare-ups and stabilization of disease; potential for inaccurate accounts due to lack of clinical follow-ups	2-
	Mediterranean Diet	2019, Barrea et al.,[20]	Case-controlled cross-sectional study	• Higher adherence to a Mediterranean Diet (MD) lowers HS severity • Diet composed of fruits, vegetables, whole grains, legumes, nuts, fish, white meat, and olive oil reduces chronic inflammation in HS • Utilizing bioelectrical impendence analysis (PhA) measurements as a tool for therapeutic intervention and management of HS	Cross-sectional design does not allow for a causal relationship between MD and HS	2-
	Dairy & High glycemic load elimination diet	2020, Dempsey et al.,[21] United States	Cross-sectional survey	• Elimination of gluten, dairy, refined sugars, tomatoes, or alcohol subjectively improves HS for some patients	Self-reported results with high potential for bias	NA

		2020, Fernandez et al.,[22] United States	Cross-sectional survey	• Avoidance of most frequently exacerbating foods: bread/pasta/rice, dairy, high-fat foods • Increased intake of reported alleviating foods: vegetables, fruit, chicken, and fish	Self-reported results with high potential for bias	NA
		2015, Danby,[23] United States	Expert Opinion	• Diets high in dairy and glycemic index have been shown to cause sebaceous gland plugging and subsequent follicular-pilosebaceous unit rupture; Avoiding these foods may help alleviate HS symptoms.	Inability to provide high-level evidence for dairy and glycemic index foods directly impacting HS	4
		2019, Maarouf et al.,[24] United States	Review article	• Avoidance of a Western diet and high mean-glycemic index foods • Increased vegetable and fruit intake	Review based on small studies and unable to provide direct correlation between dietary changes and subsequent improvement of HS	1-
		2020, Marasca et al.,[25] Italy	Letter to the editor/ Expert opinion	• A multidisciplinary approach to HS involving dietary changes due to the high insulin resistance association with HS disease severity	Inability to provide high-level evidence for dairy and glycemic index foods directly impacting HS	4
Vitamins, Minerals & Supplements	Zinc	2015, Danesh et al.,[26] United States	Expert opinion	• Apply Pyrithione zinc 1% shampoo topically in hair-bearing areas	Based on opinion and observation, no clinical study design	4
		2016, Hessam et al.,[27] Germany	Retrospective review	• Oral zinc gluconate 90mg/day tablets combined with topical triclosan 2% twice daily to reduce disease severity, erythema, and number of inflammatory nodules in Hurley Stage I & II • DLQI improvement with zinc	Retrospective design with short follow-up time; no placebo/control	1-
		2012, Dreno et al.,[28] France	3-month prospective clinical study	• Oral zinc gluconate 90mg/day may be beneficial to increase expression of innate immune markers considering the deficiency of these markers found in lesions of HS patients (Hurley Stage I & II)	Small number of patients with no placebo/ control group	2+
		2020, Molinelli et al.,[29] Italy	Controlled retrospective clinical study	• Oral zinc gluconate 90mg/day and oral nicotinamide 30mg/day can improve HS and may be a well-tolerated approach of mild-moderate disease (Hurley Stage I & II)	Retrospective nature with absence of a randomized blinded control group	2++
	Vitamin D	2020, Brandao et al.,[30] Brazil, Italy, France	Cohort study	• Vitamin D supplementation recommended based on evidence of Vitamin D insufficiency and genetic alterations involving Vitamin D pathway in syndromic HS patients (Hurley Stage III)	Vitamin D deficiency may originate from obesity, smoking or IBD associated with HS rather than HS itself; Small sample size	2-

		2015, Guillet et al.,[31] France	2-phase open label pilot study	• Vitamin D deficiency improves with subsequent supplementation and results in decreased number of active HS lesions	Absence of randomized-control group; small sample size	NA
	Turmeric/ Curcumin	2019, Silfvast-Kaiser et al.,[32] United States	Review of published and lay literature	• Turmeric may be beneficial for HS lesions in both topical and oral forms through involvement in inflammatory pathogenesis of HS	Based on online reports and lay sources; low clinical evidence	4
		2017, Perng et al.,[33] United States	Review	• Minced turmeric root as an application on HS lesions • Ingestion of diluted turmeric 3 times daily	Anecdotal success, not based on clinical evidence; specifically reviewed curcumin as a treatment for pregnant women with HS	1-
	Others	2020, Donnarumma et al.,[34] Italy	Controlled clinical study	• Supplementation with myo-inositol, folic acid & magnesium is recommended for improved efficacy of concomitant medical therapies in HS	Supplement was not the sole treatment and correlation cannot be made for the specific role it has in HS; small sample size	2+
		2019, Szántó et al.,[35] Hungary	Expert opinion	• No sufficient evidence to recommend probiotics for HS	Opinion based article	4
Traditional Chinese Medicine	TCM	2013, Feng et al.,[36] China	Controlled clinical study	• TCM in combination with Western medicine is more effective for HS, rather than Western medicine alone • Perianal HS lesions specifically show improvement with TCM (acupuncture, manual therapy & Chinese herbal medicine)	Small sample size; TCM was analyzed with Western medicine in a combined approach rather than its individual efficacy	2+
	Heshi-fire needling	2018, Li et al.,[37] China	Expert Opinion	• Needle acupuncture with Heshi-fire needling technique promotes healing of HS lesions • Can be combined with Chinese herbal medicine	Low clinical evidence	4
	Battlefield Acupuncture	2020, Daveluy & Wayne state,[38] United States	Ongoing clinical trial	• Battlefield acupuncture is a form of auriculotherapy that may have potential in reducing inflammation and providing short-term analgesia in HS	Currently ongoing study and results have not been published or completed	NA (pending completion)
Ayurveda	*Navidrana & Ksharasutra* application-based approach	2021, Malavika et al.,[39] India	Case series	• Ayurvedic protocol with the use of *Ksharasutra* combined with *Kshara* application, *Ksharajala* infiltration, dressing with *Vrana ropana* drugs and *Kshalana*, can effectively manage HS symptoms	Ayurveda is not commonly practiced in the Western world, thus limitations exist with practicality and barriers in knowledge of this approach of treatment	3
		2021, Kumar et al.,[40] India	Case report	• *Ksharataila Poorana* and *Ksharasutra* application, for a total of 5 months.		3

				• Reduction in pus discharge and hardness of the axillae • Maintenance on oral *Gandakarasayana, Triphala Guggulu and Varundi Kashay*		
		2021, Sarika et al.,[41] India	Case report	• *Guggulu* based approach is effective for inter-communicating sinus tracts in HS and can improve axillary and groin abscesses		3
	Heeler-leech therapy	2020, Jagdhane et al.,[42] India	Case report	• Use of *Hirudo medicinalis* leeches with 6 sittings over a 42-day period, combined with oral ayurvedic supplements: *Tankana Bhasma* 250mg once daily and *Varuna twaka churana* 3g twice daily		3
Wound Care	Manuka honey	2018, Braunberger et al.,[43] Australia, Germany	Review article	• Manuka honey impregnated dressings recommended for recurrent infections and HS wounds refractory to healing	Based on available studies analyzing wound care dressings in HS patients with low levels of clinical evidence	1-
Mental Health	Support groups and coping strategy therapy	2011, Esmann et al.,[44] Sweden	Qualitative study	• Support groups and therapy focused on coping strategies and improving quality of life in HS is recommended	Based on interviews rather than quantitative improvement in HS	4
	Management of depression & anxiety	2019, Machado et al.,[45] Canada	Systematic review	• High prevalence of depression and anxiety in HS warrant appropriate mental health counseling and management	Inability to directly relate management of depression and anxiety to improvement in HS	1-
	Cognitive behavioral therapy (CBT) and Acceptance and Commitment therapy (ACT)	2021, Savage et al.,[46] United States	Review article	• CBT & ACT can reduce reactivity to pain and distress associated with depression in HS patients	Suggested HS-pain algorithm requires further investigation in a clinical setting; proposed mechanism has limited clinical correlation without subsequent trials	1-

* Evidence Levels based on Scottish Intercollegiate Guidelines Network (SIGN) grades for evidence[15]:
1++ High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+ Well conducted meta-analyses, systematic reviews or RCTs with a low risk of bias
1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++ High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a low risk of confounding bias and high probability of causal relation
2+ Well conducted case control or cohort studies with a low risk of confounding bias and a moderate probability that the relationship is causal
2- Case control or cohort studies with a high risk of confounding bias and a significant risk that relationship is not causal
3 Case reports, case series
4 Expert opinion

tokines found in HS lesions and activate nicotinic acetylcholine and aryl hydrocarbon receptors which suppress the Notch signaling pathway, implicated in the pathogenesis of HS.[16] Although no causal relationship can be delineated, this pathophysiologic mechanism may serve as an underlying explanation to the high rates of association between smoking and HS. Approximately 70-75% of patients with HS smoke cigarettes and 10-15% have a previous history of smoking.[8] A recent meta-analysis by Acharya et al. in 2020 found that patients with HS were about 4 times more likely to be smokers. This emphasizes the need to screen patients with HS for active smoking status.[17] Further, a dermatology center in Singapore found that a structured pharmacist-led smoking cessation clinic can be effective in reducing smoking rates and such services can be an effective part of a holistic management of dermatologic diseases.[20] A combination of tobacco use screening and assistance with smoking cessation resources provided by dermatology clinics may have a role in decreasing severity and associated morbidity of HS.

In addition to smoking cessation, weight loss is a significant lifestyle modification that can be of benefit to patients with HS. Mechanical friction and systemic low-grade inflammation of obese habitus can serve as a nidus for HS development.[47] In a case study by Boer J., a 33-year-old female with a BMI over 30 kg/m^2, a period of weight loss with reduction of 32kg significantly improved the abdominal lesions. Significant skin-to-skin friction of the lower abdomen triggers HS lesions and weight loss can lead to obvious reduction in overall HS activity, as demonstrated in this case.[47] In addition to mechanical friction, obesity induces an inflammatory state in which the pro-inflammatory cytokines in HS are amplified and contribute to systemic inflammation.[19,47] Although weight loss can lead to substantial improvement in HS, too much weight loss may exacerbate symptoms, if there is a pronounced increase in skin folds.[18] Lifestyle interventions including substantial weight loss and smoking cessation have led to both subjective and objective improvements in symptom severity in HS patients.[48]

3.2. DIETARY ALTERATIONS

Brewer's and baker's yeasts have been explored for their possible role in HS. Yeast intolerance has been found to be present among patients with HS.[21,49] The first paper exploring the role of yeast intolerance and HS by Cannistrà *et al.* in 2013, studied 12 patients with axillary and perianal fistulas that underwent surgical excision or localized treatments followed by dietary intervention. All 12 patients had a serology-proven reaction to brewer's yeast and wheat (anti- *Saccharomyces cerevisiae* antibodies) and were put on a controlled brewer's yeast-free diet for 12 months with monthly follow-ups.[21] The diet demonstrated stabilization of their clinical symptoms with lesion regression over the treatment period. All patients studied demonstrated an immediate recurrence of skin lesions following consumption of foods containing brewer's yeast or wheat. Additionally, the patients demonstrated a return of their quality of life and activities with the controlled yeast-free diet.[21]

In a follow-up study by Aboud et al., a group of 185 patients were followed for 6 years during which 37 patients were treated with a brewer's and baker's yeast definitive exclusion diet followed by operative intervention. The diet excludes the ingestion of all bakery products, vinegar, black tea, soy sauces, beer, wine, fermented cheeses, and mushrooms.[49] The remaining 148 patients in the study were treated with traditional medical interventions involving antibiotics and immunosuppressive therapies. The patients self-reported their control of flareups and disease stabilization, active smoking, and weight loss status. In the yeast-exclusion diet group, 70% of the patients reported an improvement in HS symptomatology without any other treatment. Further, 87% reported an absence of flareups after the yeast-free diet. Immunologic testing in these patients showed intolerance to yeast, wheat, and cow's milk. Patients who required surgery following this diet required remarkably less invasive operative procedures. The absence of recurring flareups with the yeast exclusion diet among these patients, in addition to immunologic intolerance, suggests a link between food intolerance and its potential implication in the pathogenesis of HS.[49] With the hypothesis of underlying gut dysbiosis in HS following the link that was made with Crohn's Disease, there is increasing evidence that inflammatory conditions benefit from certain dietary modifications.[22]

The Mediterranean diet (MD) is widely recognized for its anti-inflammatory potential and has been examined in the multidisciplinary approach to HS. The MD characteristically consists of a high intake of fruits and vegetables, whole grains, legumes, nuts, fish, white meats, and olive oil.[23] In a case-controlled, cross-sectional study by Barrea et al., 41 HS patients and 41 control subjects were followed to investigate the relationship between body composition and adherence to MD with corresponding severity of HS. Body composition was measured by bioelectrical impendence phase angle measurements (PhA) with PREDIMED as the questionnaire utilized to assess adherence to the MD. Clinical severity of HS was measured by the Sartorius HS score. The multivariate analysis found that the PhA and PREDIMED scores indicating body composition and adherence to MD respectively, were major determinants of the HS Sartorius score.[19] Higher adherence to the MD was found to be associated with a lower severity of HS with a lower Sartorius score. Further, since the MD has an anti-inflammatory potential, the ox-LDL level can be monitored as a marker of oxidative stress and chronic inflammation. The ox-LDL levels in this cohort of patients demonstrated a positive correlation with clinical severity of HS and a negative correlation with adherence to the MD, thereby constituting the potential role for MD in the management of patients with HS.[19]

Dietary alterations such as reduction in dairy, high-fat and glycemic index foods are another method reported in the literature by which some relief of HS symptomatology has been documented. In a cross-sectional survey by Dempsey *et al.* on dietary alterations by patients with HS, a majority of patients reported alteration of at least one food from their diet. Gluten, dairy, refined sugars, tomatoes, and alcohol were among the top reported elimina-

tions, from which some participants reported the change to alleviate their symptoms.[24] Fernandez *et al.* confirmed similar findings with a cross-sectional survey reporting the most reported exacerbating foods are sweets, bread/pasta/rice, dairy, and high-fat foods, while alleviating foods include vegetables, fruit, chicken, and fish.[25] Diets high in dairy and glycemic index have been shown to cause sebaceous gland plugging and subsequent follicular-pilosebaceous unit rupture.[50] Dairy products contain insulin-like growth factor-1 (IGF-1), whey and simple carbohydrates, as well as 5α-reduced dihydrotestosterone (DHT), which subsequently increase insulin and induce opening of androgen receptors that play a role in HS. William Danby reports a personal series in this article in support of this pathophysiology, demonstrating an 83% improvement utilizing a dairy-free diet in 47 patients, none of which reported worsening.[50] Further, HS has been associated with metabolic syndrome, suggesting that a Western diet has a negative impact on the disease and contributes to the pro-inflammatory state of HS.[26] Marasca *et al.* demonstrated through a homeostasis model assessment of insulin resistance that HS patients were significantly affected by insulin resistance, and there was a correlation with disease severity, glucose rate and body mass index (BMI).[27] Dietary patterns implicated in the pathophysiology of HS indicate that evaluating individual nutrition status can be a pivotal component of alternative treatments to HS. Eliminating yeast-containing food groups, dairy and high-glycemic index foods, or utilization of the MD may be of benefit to patients with HS. Further research and large-scale randomized trials are needed to evaluate if specific dietary interventions are clinically efficacious in the alleviation of HS symptoms.

3.3. VITAMINS, MINERALS & OTHER SUPPLEMENTS

ZINC

Zinc is a cofactor that plays a role in innate immunity of the skin and has been found to be specifically involved in cutaneous inflammatory manifestations.[28] Zinc gluconate use in HS has shown anti-inflammatory effects.[28] Pyrithione zinc 1% is a topical antifungal agent with antibacterial effects with anti-proliferative, anti-inflammatory and anti-androgenic properties. One report suggests its use in hair-bearing areas which are prone to colonization by bacteria and yeast.[51]

Hessam *et al.* conducted a retrospective review of 66 patients with HS in Hurley stage I and II who were treated with oral zinc gluconate 90mg/day and topical triclosan 2% twice daily for 3 months. They established zinc significantly decreased disease severity, erythema, and number of inflammatory nodules through a substantial improvement in the modified HS Score (mHSS) and Dermatology Life Quality Index (DLQI).[29] There was no significant difference in the number of fistulas or the intensity of pain, and since topical triclosan was utilized alongside, the suppressive effects of zinc could not be isolated.

Dreno *et al.* also examined the effects of oral zinc gluconate for 3 months in a prospective analysis of 12 patients. Skin biopsies were performed at baseline and after treatment with 90mg/ day oral zinc gluconate for 3 months to examine innate immunity markers. Compared to normal skin, lesional HS skin showed significant downregulation of innate immune markers (except IL-10), which subsequently increased after three months of zinc treatment.[52] Increased expression of these inflammatory innate immune markers following zinc treatment provides evidence contradictory to the anti-inflammatory effects documented by Hessam *et al*. and instead demonstrate a pro-inflammatory effect of zinc.[52,53] This effect may be desirable for HS due to the deficiency of innate immune markers involved in the chronic inflammatory state. Given the anti- vs. pro-inflammatory effects of zinc in these studies, clinical trials are needed to determine both formulation and dosage of zinc that may provide a therapeutic effect on HS lesions.[53]

A more recent study by Mollinelli *et al.* investigated the efficacy of oral zinc and nicotinamide as maintenance treatment in mild-moderate HS. Ninety-two HS patients with Hurley Stage I and II were previously treated with oral minocycline and subsequently divided into a treatment and a control group. The treatment group was maintained on 90mg zinc gluconate and 30mg nicotinamide orally once daily for 90 days. Patients in the treatment group reported a remarkable improvement in DLQI, Visual Analog Scale (VAS), International Hidradenitis Suppurativa Severity Score System (IHS4) scores compared to the control group at 12 and 24 weeks.[54] Zinc, therefore, may have a higher efficacy when combined with nicotinamide supplementation in patients with mild to moderate HS. For patients placed on long-term zinc supplementation, monitoring for signs of anemia and co-administration of copper are recommended.[30]

VITAMIN D

Vitamin D is an important component of skin homeostasis, regulation of proliferation, and differentiation of epidermis and adnexal structures, especially hair follicles.[31] Vitamin D increases the expression of Toll-Like Receptor 2 (TLR2) and anti-microbial peptides. Importantly, vitamin D has an inhibitory roll in T cell response to IL-1, IL-2, IL-6 and interferon-γ, preventing evolution to chronic inflammation.[32] Therefore, vitamin D may have a role in the deficient innate immunity and follicular obstruction of HS. A study by Brandao *et al*. analyzing genetic changes related to syndromic HS patients utilized genomic DNA extraction and whole exome sequencing on 5 patients in Hurley stage III. All 5 patients presented high levels of variant density in the vitamin D pathway and some of them with deleterious and damage impact.[55] Subsequently, vitamin D serum levels were measured, finding all patients with low levels. These findings provide some support for the involvement of vitamin D insufficiency with a recommendation to supplement in HS patients.[55]

In further support of this evidence, Guillet *et al.* conducted a pilot study consisting of two phases whereby one phase determined vitamin D dosage and the second phase tested vitamin D supplementations. The first phase consisting of HS 22 patients found that 100% of patients had a vit-

amin D deficiency with a median vitamin D level of 12.7ng/mL and severely deficient in 36% of patients (<8ng/mL). Deficiency severity was correlated with severity of Hurley's grade and with absence of family history of Verneuil's disease. In the second phase, 14 out of 22 patients with HS were supplemented with vitamin D based on their levels at baseline, 3 months, and 6 months. Among these 14 patients, deficiency completely regressed in 10 patients at month 3. The study found efficacy of vitamin D at month 6 with a 75% decrease in the number of nodules (p = 0.01133).[33] Although this was not a randomized-controlled study and had a very small sample size, the evidence sheds light on the potential for improvement of HS with vitamin D supplementation, particularly with proven deficiency and mechanistically improving skin innate immunity.

TURMERIC

Turmeric is a natural plant root which has been studied for its anti-inflammatory properties. Various online sources and lay literature claim that turmeric is beneficial for HS lesions in both oral and topical forms.[34] Studies have shown curcumin, the principal curcuminoid, regulates and modulates immune cells such as T-lymphocytes, macrophages, dendritic cells and natural killer cells, which are involved in the inflammatory disease pathogenesis of HS.[34] According to the survey by Price *et al.* on CAM use in HS patients, turmeric/curcumin was the second most reported method utilized.[13] Despite individual reports of turmeric use, no clinical studies have been conducted specifically on the role of turmeric in HS. Nine different randomized controlled studies have found curcumin to play a role in metabolic syndrome, diabetes, and obesity, all of which have been implicated as comorbidities in HS.[35] Some of the beneficial effects of curcumin include lipid lowering effects, improved glycemic control, and reduction in concentrations of various inflammatory cytokines.[35] In a review of HS treatments in pregnant women, Perng *et al.* suggests anecdotal success with minced turmeric root as an application on HS lesions as well as ingesting diluted turmeric 3 times daily.[56] Downregulation of inflammatory cytokines by turmeric may play a role in relieving inflammation in HS patients.

OTHER SUPPLEMENTS

Oral supplementation composed of myo-inositol, folic acid and liposomal magnesium (Levgigon®) was explored in a study by Donnarumma *et. al* on a cohort of 12 HS patients over the course of 6 months. These patients were Hurley stage I and II with impaired glucose metabolism and a BMI of 25-29.9 and were also treated with topical clindamycin gel 1%, oral clindamycin 300mg twice daily, and oral Rifampin 600mg once daily for 6 weeks. After 6 months, the patients on supplementation showed increased efficacy when compared to those not receiving supplementation.[36] The importance of evaluating metabolic profiles in HS patients is highlighted in this study and moreover suggests that myo-inositol, folic acid and magnesium supplementation in HS can improve efficacy of concomitant therapies.[36] This study utilized a combination approach of medical management, and therefore needs further evaluation to determine if it can be efficacious in HS as a CAM method alone.

The association between HS and inflammatory bowel disease has raised the question of gut dysbiosis as a mechanism of disease exacerbation. However, there is not enough evidence to support the use of probiotics in HS.[37] Although probiotics have been studied in other cutaneous conditions and inflammatory processes, they have not been studied in HS patients.

3.4. TRADITIONAL CHINESE MEDICINE

Traditional Chinese Medicine (TCM) is derived from an ancient system of knowledge which is fundamentally defined by therapeutic procedures such as acupuncture, manual therapy, and Chinese herbal medicine.[57] A study by Feng *et al*. in 2013 analyzed treatment of perianal HS by TCM in combination with Western medicine vs. Western medicine alone. Of 48 patients, 24 were treated with TCM and Western medicine, and the other 24 were treated with Western medicine alone as the control group. The cure rate of the treatment group was 83.33% vs 50% in the control group.[38] These findings suggest that utilization of TCM may be beneficial in patients with HS, especially those with perianal lesions.

According to Li *et al*., individuals with HS cannot detoxicate and promote tissue regeneration in the realm of TCM. The "Wen-tong" therapy of "Heshi Santong" therapy is a form of needling acupuncture that can promote healing by facilitating the resistance to exogenous pathogenic factors.[58] Heshi fire needling can be combined with herbal Chinese medicine for the treatment of HS. The needling sensation and the generated heat induces a self-healing response of the body that may have potential efficacy in HS.[58] Currently, an ongoing clinical trial by Steven Daveluy and Wayne State University is investigating the role of battlefield acupuncture for the treatment of pain in HS. Battlefield acupuncture was developed in 2001 as a form of auriculotherapy where a sequence of semipermanent needles are placed in up to 5 specific spots in one or both ears in order to elicit short-term analgesia or anti-inflammatory cytokines for long term effects.[42] The study by Wayne State has a treatment group undergoing 2 treatments of battlefield acupuncture to the ears bilaterally a week apart, and a control group with a sham acupuncture.[39] The participants will be recording their pain levels every week for 4 weeks. The results of this study when completed, may have a potential impact on alternative approaches to treating pain in HS.

3.5. AYURVEDA

Ayurveda is a comprehensive approach to healthcare that originated in the ancient Vedic times of India.[41] Ayurveda classically relates HS to a term called *Nadivrana,* which encompasses pus drainage and tract formation alongside other comparable clinical symptoms to HS.[40,43,59] The management mode for *Navidrana*, is through *Ksharasutra* application which involves excision, incision, scraping, pu-

rification, and epithelialization of healthy granulation tissue utilizing ayurvedic medicine.[59] In a case series by Malavika *et al*. at the Sree Narayana Institute of Ayurvedic Studies and Research, an ayurvedic protocol was developed combining para-surgical techniques alongside "internal" medications for 2 patients. The use of *Ksharasutra* is combined with *Kshara* application, *Ksharajala* infiltration, dressing with *Vrana ropana* drugs and *Kshalana*. Both patients were effectively managed with ayurvedic treatment utilizing this protocol.[59]

A case by Kumar *et al.* reported in the journal of Ayurveda and Integrated Medical Sciences also followed the treatment modality of Ayurveda directed towards *Nadivrana* discussed above, yielding similar results. The patient had failed a number of surgical treatments including incision and drainage, as well as wide excision. This patient was treated with ayurvedic modalities, mainly *Ksharataila Poorana* and *Ksharasutra* application, for a total of 5 months. Subsequently, there was a reduction in pus discharge and hardness of the axillae with no recurrence at the 8-month follow-up and the patient was then maintained on oral Gandakarasayana, Triphala Guggulu and Varundi Kashaya.[44] Another case report in this journal by Sarika et al, sustained the underlying classical thought of *Nadivrana* and utilized a *Guggulu* based *Apamarga Ksharasutra* for inter-communicating sinus tract. *Guggulu* is derived from the *Commiphora wightii* plant and is thought to have anti-inflammatory and analgesic properties. A 19 year-old female with HS presented with lesions in the bilateral axillae and groin regions and the use of this form of Ayurveda resulted in improved axillary abscesses and complete resolution of groin lesions.[43]

Jagdhane *et al.* reported a case that explored the use of heeler leech therapy, a form of Ayurveda. Leech application is said to extract impure blood, exhibiting a bacteriostatic and bactericidal effect, along with removal of pus and toxins.[40] *Hirudo medicinalis* leeches, indicated for medicinal use in ayurvedic therapy, were applied locally in the bilateral axillae of a 48-year-old woman with axillary HS, obesity and diabetes. The patient was provided 6 sittings with leech application with an interval of 6 days between sittings, for a total of 42 days. The patient was also given two oral ayurvedic supplements, *Tankana Bhasma* 250mg once daily and *Varuna twaka churana* 3g twice daily. This intervention proved to be efficacious in reducing inflammation, swelling and discharge in this case. No recurrence was seen after 3 months of treatment.[40]

3.6. WOUND CARE

An often-overlooked area where the use of alternative medicine can be utilized is wound care dressings. A plant native to New Zealand, *Leptospermum scoparium,* allows for the production of manuka honey, which has antimicrobial and antioxidant properties that can be used in dressings.[45] A review by Braunberger *et al*. analyzing dressing methods in HS discussed the use of manuka honey dressings in a patient who had previously undergone surgical excision. A refractory wound was dressed with manuka-honey impregnated dressings and recurrent infection with *Staphylococcus* subsided and the wound subsequently healed.[60] There are no articles to date on the use of manuka honey as a primary alternative method of treatment. However, its properties in wound healing show promising features for patients with HS and may have a potential benefit at some point in management of lesions and non-healing wounds.

3.7. MENTAL HEALTH MANAGEMENT

HS has a significant emotional impact on patients, ultimately promoting isolation and negatively affecting mental health, leading to an overall poor quality of life. A qualitative study by Esmann *et al*. conducted on 12 HS patients over 2 years found a psychosocial impact of the disease that affected emotion, self-worth, stigmatization, intimate relations, cognition, communication, worry of continuous precautions, and economical stress. The study found a high frequency of depression among patients with HS, regardless of their coping strategies. The authors of this study suggested that patients with HS may benefit from support groups and therapy that allow them to focus on coping strategies and improving their quality of life.[46]

Further, a systematic review by Machado *et al*. showed a 16.9% prevalence of depression and 4.9% prevalence of anxiety in a cohort of 40,307 participants with HS.[61] It is well known that mental health heavily intertwines with physical health, leading to exacerbation of chronic disease states and prevention of appropriate healing. Patients with HS need long-term psychosocial support outside of traditional medical management. "Mind-body" CAMs such as meditation, hypnosis, tai chi, yoga and massage therapy are some of the methods self-reported by patients, but have yet to be studied for efficacy in HS.[62] Depression strongly impacts pain perceptions. Thus, modalities such as cognitive behavioral therapy (CBT) and acceptance and commitment therapy (ACT) can be utilized in HS patients to reduce pain and psychological distress.[63] ACT emphasizes reducing reactivity to pain distress and may be more beneficial than CBT in those with poorly controlled HS due to the associated physical limitations that may impact CBT.[63] Further studies are needed to examine CBT and ACT's efficacy in treating chronic pain in HS patients.

4. DISCUSSION & CONCLUSION

HS is a debilitating chronic disease that affects individuals in various aspects of life. Finding efficacious alternative therapies is often difficult with the lack of clinical evidence and support from medical providers. This review yielded many articles with a low to moderate quality of evidence, but no conclusive recommendations can be made without high quality clinical trials.

Lifestyle modifications have become increasingly supported due to known associated comorbidities in HS such as obesity and diabetes. Smoking is a well-established risk factor for HS. Thus, smoking cessation is highly recommended. Weight loss has shown positive clinical response due to reduction in areas of friction and overall inflammation. In the realm of dietary alterations, brewer's and

baker's yeast elimination is recommended with some evidence for utilization before surgical management, and some evidence prior to any medical management to reduce invasive modalities of conventional treatment. Given the difficulty of following such a diet, patients should be screened for *saccharomyces cerevisiae* antibodies and recommendations should appropriately be made in patients with a positive serology. Elimination of high-glycemic load and dairy food groups and the Mediterranean diet has been reported to contribute to a reduced disease severity.

Vitamins, minerals, and supplements with the most reported literature for positive clinical effects in HS include zinc, vitamin D, turmeric and a combination of magnesium, myo-inositol, and folic acid. Preliminary evidence supports the use of zinc in HS. However, the dosage and form of zinc is debated, along with its anti- vs. pro-inflammatory effects on the deficient innate immunity of HS lesions. Vitamin D has proven to be frequently deficient in HS patients and has warranted subsequent supplementation with some positive results. However, data has been inconclusive in correlating vitamin D deficiency to HS itself rather than associated smoking, obesity etc. Curcumin is known to improve glycemic control and reduce inflammatory cytokines, both of which may be beneficial in patients who have associated HS comorbidities. Clinical studies on probiotics are lacking. Lastly, there is some support for magnesium, myo-inositol, and folic acid, as a combination pill, to improve efficacy of concomitant medical treatment in a small controlled clinical study.

Traditional Chinese medicine has shown encouraging results when combined with Western medicine. Heshi-fire needling and battlefield acupuncture are forms of TCM that have been used in HS and need further studies to determine true efficacy. Multiple case reports of Ayurvedic treatment modalities have shown reduction in HS lesions, inflammation and an improvement in abscesses and sinus tract formation. These modalities may be utilized by those with expertise in the field. However, many barriers exist to providing these treatments in the United States. Manuka honey dressings have shown to improve recurrent infections in non-healing wounds of HS and may be considered for management of refractory wounds. Finally, support groups and mental health therapy are recommended for all HS patients due to the large percentage of patients with depression, anxiety and distress associated with the disease.

Overall, a multi-disciplinary approach to HS involves assessing metabolic risk factors and the role of associated comorbidities in targeting management. Further, CAMs such as lifestyle changes and dietary control can benefit patients and are recommended in a comprehensive management plan. Some of the modalities discussed in this review may be beneficial with concomitant conventional treatments and may achieve desirable outcomes for patients. Importantly, many patients utilize these CAMs, regardless of physician support. Thus, medical providers should be informed on these alternative treatments to avoid improper use. While the findings discussed above are encouraging, it may be premature to provide concrete evidence-based recommendations based on current literature. Therefore, further investigation into the clinical indications and potential adverse events of various CAMs for the management of HS is warrnated. The preliminary reports and evidence discussed in this review support the need for large-scale clinical studies for the use of CAMs in HS.

5. LIMITATIONS

This systematic review has several limitations due to the lack of studies with high levels of evidence. Most of the studies had small sample sizes, lacked control groups, and carried a significant risk that there was a low causal relationship between intervention and HS improvement. We were unable to place limitations or screen for specific outcomes such as an HS Sartorius score, as most of the studies did not use objective outcome measurements. Many articles included subjective patient-reported improvements and lacked a developed method or scale for assessing HS severity. Therefore, this review has a wide scope of inclusion, which should be taken into consideration for future research on this topic. None of the studies were RCTs measuring the effect of a CAM intervention on HS. With the quantity of observational studies, case reports and expert opinions, most evidence was of low to moderate quality.

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The authors have no conflicts of interest to declare that are relevant to the content of this review.

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