Balancing Acne: The Review of Psychological and Physical Therapies in Stressful Environments

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This paper explores the intricate relationship between stress and the skin inflammation of acne. Chronic stress triggers the activation of the hypothalamic-pituitary-adrenal (HPA) axis, culminating in the release of stress hormones that modulate immune function and disrupt inflammatory signaling pathways, thereby exacerbating skin inflammation of acne and perpetuating immune dysregulation. While conventional treatments predominantly target the microbial elements of skin inflammation, emerging research highlights the pivotal role of psychological interventions in optimizing therapeutic outcomes. Techniques such as biofeedback-assisted relaxation have demonstrated efficacy in reducing stress and improving skin health parameters as it promotes individuals to regulate their stress response, fostering resilience against stress-induced exacerbation of acne. Additionally, innovative therapeutics such as phototherapy, leveraging light-based technologies such as lasers and light-emitting diodes (LEDs), offer a non-invasive approach to modulating inflammatory responses and targeting microbial overgrowth. By raising awareness about the intricate interplay between stress and skin inflammation of acne and reviewing a multidisciplinary treatment approach, clinicians can optimize patient outcomes and enhance overall skin health. This literature review examines the mechanisms by which stress interacts with acne, and evaluates therapies in oral antibiotics, topical therapies, biofeedback therapy and phototherapy, and the limitations and side effects associated with these treatments.

Keywords: Stress, Low-Level Laser Light Therapy, Skin Inflammation, Acne, Biofeedback, HPA Axis

Introduction

Acne is a common skin condition that affects individuals of all ages in which stress has been suspected to trigger or exacerbate acne[1]. Stress represents the body's reaction to a wide range of mental, emotional, and physical pressures encountered in daily life which can significantly influence physiological processes, including skin health. When individuals experience stress, the hypothalamic-pituitary-adrenal (HPA) axis- a central stress response system- is activated, leading to the secretion of stress hormones that can profoundly affect the skin's function and integrity. When stress is acknowledged the hypothalamus secretes corticotropin-releasing hormone (CRH). CRH stimulates the pituitary gland to release adrenocorticotropic hormone (ACTH), which in turn prompts the adrenal cortex to produce glucocorticoids, primarily cortisol[2]. The elevated cortisol levels modulate the immune system by suppressing the production of pro-inflammatory cytokines and altering the activity of various immune cells, such as T lymphocytes and macrophages[3]. This modulation can lead to an imbalance in cytokine production, promoting a pro-inflammatory environment that exacerbates skin conditions. However chronic stress can lead to the dysregulation of the HPA axis, where the immune system becomes overactive or improperly regulated. This dysregulation favors a pro-inflammatory state, contributing to the development and persistence of skin inflammatory conditions[3]. Substances of CRH, ACTH, and cortisol can influence skin proliferation, differentiation, and apoptosis, disrupting the skin barrier function, increasing the susceptibility to microbial invasion and irritants that promote inflammation[4]. In instances where individuals struggle with mental health issues such as anxiety and depression, there is an observable intensification of skin inflammation symptoms, which highlights the intertwined nature of mental health and dermatological conditions[5]. This bidirectional relationship suggests that not only can mental health conditions exacerbate skin issues, but chronic skin conditions can also contribute to psychological distress, creating a cyclical effect that complicates treatment. The conventional treatment strategy, predominantly centered around the use of antibiotics, primarily addresses the microbial components of skin inflammation for acne. While antibiotics can mitigate bacterial inflammation- which may be a source of stress and subsequent psychological distress- they do not directly address stress-induced inflammation unless it is secondary to the infectious condition. Recognizing the complex relationship between chronic stress, mental health disorders, and skin inflammation for acne is vital for developing effective therapeutic strategies. This understanding leads to integrating psychological and physical therapies, which can be crucial

for effectively mitigating the impact of stressful environments that contribute to bacterial-induced acne. Such an integrated approach aims to alleviate the visible symptoms of acne and tackle the root causes embedded in the intricate dynamics between mental well-being and dermatological health7. Chronic stress and mental health conditions can disrupt inflammatory responses, making it essential for individuals with prolonged acne to consider a treatment of combined psychological and physical therapies.

Method

This literature review aims to explore the relationship between chronic stress and skin inflammation of acne and assess the potential benefits of integrating psychological and physical therapies for treatment. The databases PubMed and the National Institutes of Health (NIH) were used to identify relevant sources.

Search Strategy

Keywords and phrases used in the search included:

1. `chronic stress AND skin inflammation`
2. `low-level laser light therapy`
3. `HPA axis AND stress`
4. `psychological interventions AND dermatology`
5. `Acne`
6. `Atopic Dermatitis`

Studies published between 2000 and 2023 were included, with the exception of one seminal study from 1981 due to its pertinent information on biofeedback therapy and skin health.

Inclusion and Exclusion Criteria

Inclusion Criteria

1. Peer-reviewed studies.
2. Articles discussing stress-related skin inflammation.
3. Sources investigating psychological or physical therapies for dermatological conditions.
4. Research involving human subjects.

Exclusion Criteria

1. Non-English language articles.
2. Studies focusing solely on animal models without human clinical correlation.
3. Publications not accessible in full text.

Selection Process

1. Titles and abstracts were screened for relevance.
2. Full-text articles were reviewed to ensure they addressed the link between stress and skin health, as well as therapeutic interventions.
3. References within selected articles were examined to identify additional pertinent sources.

Data Extraction and Synthesis

Information was extracted on the following key topics:

1. Types and effects of stress on skin inflammation of acne.
2. The role of the hypothalamic-pituitary-adrenal (HPA) axis in mediating stress responses leading to skin inflammation.
3. Common treatments for acne and their potential side effects.
4. The efficacy and biological mechanisms of low-level laser light therapy.
5. The impact of psychological interventions, such as biofeedback therapy, on skin health of acne.

A narrative synthesis approach was employed to integrate findings from various studies, providing a comprehensive overview of the current understanding of the topic.

Potential Biases and Limitations

As a literature review rather than a systematic review, this study may be subject to selection bias due to the non-systematic search strategy and subjective selection of sources. Limitations include:

1. Possible omission of relevant studies not indexed in the databases searched.
2. Potential bias towards studies with positive findings.
3. The inherent limitation of not performing a quantitative meta-analysis to statistically assess effect sizes.

This literature review synthesizes existing research to provide a comprehensive understanding of how chronic stress contributes to skin inflammation of acne and how integrating psychological and physical therapies may offer more effective treatment strategies. The findings aim to inform both clinical practice and future research directions.

Results

Acute and Chronic stress and the Effects on the HPA axis

Stress, encompassing physiological and psychological responses, significantly impacts overall well-being and various health aspects, including skin conditions like inflammation. Stress arises from internal and external stressors, whether from uncontrollable environmental and societal factors or controllable personal behaviors such as sleep deprivation. Stress can be classified as either chronic or acute[3].

Chronic stress involves sustained stressors over a prolonged period, whereas acute stress stems from daily minor occurrences. Acute stress triggers immediate physiological responses, including activation of the HPA axis, leading to transient changes in skin function such as increased temperature and metabolic rates[3]. The HPA axis, a neuroendocrine system, regulates immune responses and the nervous system's reaction to stressors[2].

Under stress, the skin turns pale due to elevated blood pressure and heart rate caused by nervous system activation. In contrast, chronic stress leads to prolonged HPA axis activation, resulting in hormonal imbalances and immune system alterations that have more profound effects on skin health.

Chronic stress alters the immune response compared to acute stress, leading to an adapted immune response pattern[3]. The mechanisms of immune system alteration under chronic stress first starts with inflammatory cytokines released in accordance to chronic stress to suppress cellular immune responses, resulting in Th2 dominance, which involves antibody production to prevent excessive inflammation. However, Th2 dominance weakens the immune response, making the body less effective against new threats and potentially failing to eliminate cells like tumor cells[3], as seen in Figure 1.

This immune response dysregulation disrupts the balance between pro-inflammatory and anti-inflammatory cytokines, favoring a pro-inflammatory state. The release of pro-inflammatory cytokines can contribute to the development of skin inflammation[3].

Demonstrating how psychological stressors can manifest particularly in the skin. Psychological interventions can modulate the stress response and restore immune balance, with techniques such as MBSR which have been shown to reduce pro-inflammatory cytokine levels, which decreases skin inflammation[6].

Connection Between PTSD and Dermatology

Mental disorders such as post-traumatic stress disorder (PTSD) can influence stress levels and have a significant relationship with dermatology. PTSD is a syndrome that appears in individuals who are exposed to a traumatic event[7]. "Approximately 60% of the population will experience at least one traumatic stressor in their lifetime," while "the lifetime prevalence for PTSD is only about 6.8%"[8].

PTSD can cause a set of intrusion symptoms, which are psychosomatic effects resulting from emotional and physical neglect, direct effects of physical or sexual abuse, and catastrophic life events[9]. The intrusion symptoms can manifest as traumatic flashbacks re-experienced by the body with reactions such as pain, itching, and other sensations. For instance, patients with PTSD who had a traumatic event like a stabbing can feel itching and burning sensations in the area where the stabbing occurred[9]. These intrusion symptoms can lead to behaviors such as skin picking, which develop and cause dermatologic effects in addition to being stressors.

Thus, elevated levels of inflammatory biomarkers and impaired barrier function are due to the HPA axis's hyperresponsiveness in PTSD, similar to the response from chronic stress in the immune system[4]. This demonstrates how psychological stressors can manifest physically, particularly in the skin, and underscores the need for treatments that address both psychological and dermatological aspects.

Psychological interventions, particularly trauma-focused therapies like Eye Movement Desensitization and Reprocessing (helps individuals heal from trauma by recalling distressing memories while engaging in guided bilateral eye movements or other forms of rhythmic stimulation.) and Cognitive Processing Therapy (aids individuals in overcoming PTSD by identifying and reframing unhelpful thoughts and beliefs associated with traumatic events.), have been effective in reducing PTSD symptoms[10]. By alleviating PTSD symptoms, these interventions can indirectly improve skin conditions exacerbated by stress and trauma. Integrating psychological treatments for PTSD can, therefore, have a dual benefit, improving mental health and reducing stress-induced skin manifestations of acne.

In recent years, there has been a study on the course of acne in healthcare workers and its risk factors. Out of 172 healthcare workers, 45.35% reported that their acne complaints had increased[11]. When analyzing the study, stress was a prominent factor to consider, as it had been noted in studies before that 97% of the participants reported increased stress and acne, reflecting a correlation between the two[11]. This real-world evidence highlights the significant impact of stress on skin conditions, especially in high-pressure environments like healthcare during a pandemic.

Implementing stress management programs in such settings can be highly beneficial. Techniques like resilience training

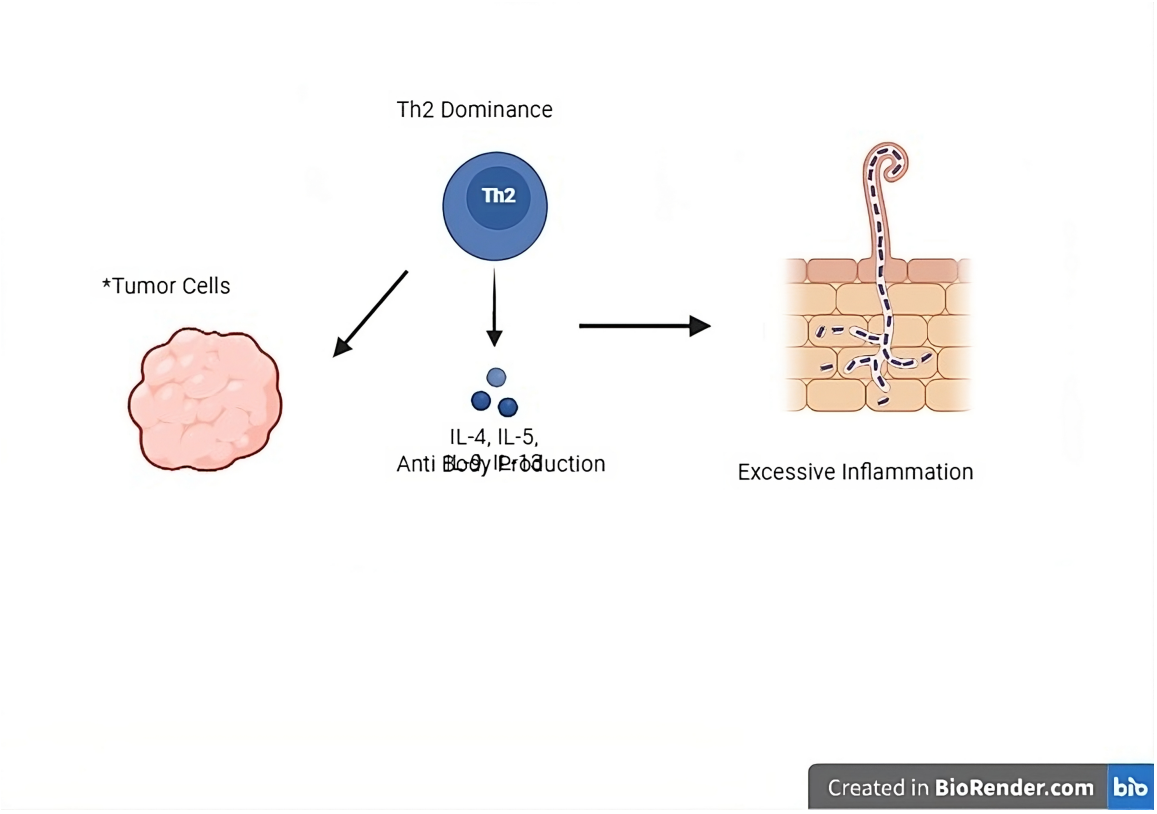

Fig. 1 Illustration of TH2 antibody production working towards tumor cells and inflammation[3].

and mindfulness meditation can reduce perceived stress levels among healthcare workers, potentially mitigating the exacerbation of acne and other stress-related skin conditions[12].

Barrier Functions of the Skin and Reactive Oxygen Species

Stress-induced alterations in skin physiology extend beyond hormonal effects, profoundly influencing the skin's structural and functional integrity. The elevated levels of inflammatory biomarkers and impaired barrier function resulting from the hyperresponsiveness of the HPA axis, as observed in chronic stress, set the stage for a deeper understanding of how stress profoundly influences the skin's defensive capabilities.

Acute internal stressors can affect multiple skin functions such as the epidermal physical barrier, the skin's defense mechanism, the neuroendocrine, and thermoregulation[4]. The epidermal physical barrier's primary function is to defend against extrinsic factors such as microbes and "maintain stratum corneum hydration by preventing unregulated trans-epidermal water loss"[4].

The first step in a repair response to acute stressors is the secretion of contents of water barriers from the outer stratum. However, stress can impair these repair mechanisms, leading to increased transepidermal water loss and dehydration of the skin. Then, the skin barrier utilizes cell growth and an increased adhesion molecule expression, which facilitates the attachment of immune cells to sites of inflammation, contributing to an immune response[4]. However, chronic stress can disrupt cell proliferation and adhesion processes, weakening the barrier and making the skin more susceptible to damage overall.

The skin's defense mechanisms start with a biochemical defense against acute stress to maintain cellular homeostasis. DNA repair and maintaining hydration levels ensures the skin remains moisturized and functional with osmolyte strategies[4]. Additionally stress can hinder DNA repair mechanisms and osmolyte balance, leading to an impaired skin function.

There is then an increase in reactive oxygen species- reactive molecules containing oxygen that are produced in cellular processes and increase in response to stressors- which prompts an expression in matrix metalloproteinases- an enzyme that has a role in the breakdown of extracellular components such as collagen- that breaks down collagen- a protein that supports the structural integrity of tissues[4]. The breakdown of collagen can be weakened by antioxidants that help counteract the effects of reactive oxygen species[4].

Increased ROS levels due to stress contribute to oxidative stress, which accelerates inflammation and causes cell death in the skin as part of the cell's defense against stress. This

degradation of collagen impairs the skin's structural integrity and inhibits the wound healing process

The skin's neuroendocrine cells produce hormones, neurotransmitters, and neuropeptides, which are part of the neurogenic inflammation as they activate the HPA axis due to attracting immune cells, and exacerbate inflammation[4]. While the skin's neuroendocrine system sheds light on its role in neurogenic inflammation, there is also a consideration of the parallel influence of oxidative stress.

Oxidative stress is a disorder between the production and storage of oxygen-reactive species. Oxidative stress reactions produce biochemical components, such as reactive oxygen species (ROS) and reactive nitrogen species (RNS)[13].This imbalance leads to cellular damage, lipid peroxidation, and activation of inflammatory pathways.

Oxidative stress, with its imbalance, can then accelerate inflammation and cause cell death in the skin as a part of cell defense against stress[13]. Patients with atopic dermatitis often exhibit high levels of ROS, linking oxidative stress to poor progression and development of atopic dermatitis.

Additionally, stress hormones like cortisol and catecholamines are critical hormones released during stress that interact intricately with the skin and immune cells. Cortisol suppresses the activity of immune cells such as T lymphocytes and macrophages, leading to a decreased ability to fight off pathogens and altering the body's response to antigens. This then also influences cytokine production, shifting the balance between proinflammatory and antiinflammatory cytokines[2].

Chronic elevation of cortisol inhibits fibroblast proliferation and collagen synthesis, essential for skin strength and wound healing, resulting in delayed wound healing and skin atrophy. Catecholamines, including adrenaline and noradrenaline, are hormones produced during stress that plays a role in the "fight or flight"response, which can reduce blood flow to the skin, impairing the skin's function and healing[3].

Catecholamines also can activate mast cells, leading to the release of histamine and other inflammatory mediators contributing to itching and inflammation. As they sensitize nerve fibers, lowering the threshold for pain and itch sensations[3]. For example, the itch-sensing threshold can be decreased, building up skin inflammation with increased itching while also impairing the skin barrier function, wound healing, and suppressing immunity.

At the same time, the skin employs the immune system to combat stress. However, an abnormality in immune system regulation involving inflammatory cytokines alters immune cells, which impacts inflammation. This abnormality also results in a decline in the skin's healing with the repair and restoration processes against skin inflammation[3].

The more common skin inflammatory disorders directly influenced by the decreased itch-sensing threshold and the impairment of the wound healing processes are acne, atopic dermatitis, and psoriasis. These conditions are often exacerbated by stress, creating a cycle where stress worsens the skin condition, and the skin condition increases stress levels[14]. Addressing these multifaceted effects of stress suggest the use of therapies that target both physiological and psychological aspects to break the cycle of stress-induced skin inflammation of acne.

Oral Antibiotics and Topical Therapies' Potential Side Effects

Despite the critical role of the skin's barrier functions and immune responses in combating inflammation, conventional treatments often focus solely on addressing bacterial components of skin conditions. One of the most common treatments in the dermatologic field is antibiotics, "despite an overall decrease in antibiotic prescribing in dermatology over the past decade, US dermatologists continue to prescribe antibiotics at higher rates than providers of other specialties[15]." This overprescription contributes to a growing risk of resistant infections and treatment failures[15]. The most commonly prescribed antibiotics are oral for skin and soft tissue infections and chronic inflammatory skin conditions. However, there is antibiotic resistance among C. acnes with the use of oral antibiotics. As a result, many in the medical field advocated decreasing the use of antibiotics, and recent acne guidelines have recommended limiting the use[16].

It was found that from 2008 to 2016, infections and surgical visits were associated with short antibiotic courses. In contrast, diseases such as acne and rosacea were associated with them, which supports the need not to overuse antibiotics in surgical settings. So, research efforts aim to understand how antibiotic prescription in dermatology leads to antibiotic resistance. Evidence from some of these human microbiome studies suggested that the use of antibiotics turns on the expansion of antibiotic resistance in skin bacteria even if nonlethal concentrations of antibiotics are subjugated on skin bacteria[15].

Hence, there are alternative therapies and medications to defend against acne, such as topical therapies[16]. An example of topical therapy would be retinoids, as they reduce hyperpigmentation and help rebuild the papillary matrix between the outermost and most profound layers of the skin[17]. However, retinoids are not universally effective, as in the case of pregnant women; retinoids should be avoided due to their teratogenicity in oral form[18].

Another controversial retinoid is specifically isotretinoin, as many drugs regulatory agencies across the world have warnings about the risk of potential psychiatric effects, including depression and suicide[19]. In 2005, the FDA would have a warning for the side effects that would include psychosis, aggression, depression, and suicide.

It is noted that there is disagreement between dermatologists on these psychiatric effects as subjects measured by Positron Emission Tomography Fluorodeoxyglucose showed a signifi-

cant reduction in the brain region that is associated with depression (orbitofrontal cortex metabolism) after four months of isotretinoin use[19]. In comparison, a study concluded that isotretinoin treatment of acne had improved depressive symptoms and that there were clear indications of improvements in moods that were statistically significant[19]. As well, no suicide risks were reported during a follow-up of the case. In another case study, a topical treatment group compared to the isotretinoin group, and psychological test scores showed that there had been more significant improvement in the isotretinoin after four months, with no increases in depression and anxiety symptoms[19].

In addition to the potential side effects and antibiotic resistance, there would be more alternatives available. One includes probiotics, which, unlike antibiotics, are microorganisms that help the skin without killing bacteria. However, probiotics are limited in maintaining homeostasis; inflammatory skin diseases such as atopic dermatitis, psoriasis, and acne are difficult to fully heal[20].

There is also the use of corticosteroids in acne treatment such as Prednisone which is used for severe inflammatory acne. Recommended for short-term use due to significant side effects with long-term use. Low-dose oral corticosteroids may be combined with combined oral contraceptives (COCs) for patients with hyperandrogenism.Corticosteroids act as potent anti-inflammatory agents.They inhibit pituitary adrenocorticotropic hormone (ACTH) production, lowering androgen levels[21]. Additionally, they suppress activation of androgen receptors on sebocytes, reducing excessive sebum production. However, there can be short term effects of gastric discomfort and hyperglycemia[21]. While in the long term the suppression of the HPA axis, can lead to hormonal imbalances as stated earlier[21].

Thus, patients with inflammatory acne can become severe and create scars, hyperpigmentation, and psychological damage in depression and isolation from an individual's social life, which creates a grading scale of acne with four distinctive grades. Grade 1 is when there is non-inflammatory acne, which has only closed and open comedones (small bumps); grade 2, which as many comedones, as well as papules and pustules that cause inflammatory lesions; grade 3, which has papules, pustules, and comedones, nodules, and cysts, and grade 4 which contains all of the factors but an addition to increase the severity of having scars[5].

Usually, for grade 1 and grade 2 acne, topical products of retinoids, retinoic acid, isotretinoin, and comedolytics are applied. This comes with the possible side effects mentioned before, such as flaking, dryness, burning, and itching. As well, retinoids are deactivated when interacting with sunlight[5]. However, in grades 3 and 4, acne can be treated with oral antibiotics such as doxycycline and topical products. This contains similar hepatotoxic effects from before, such as itching, but also contributes to fatigue, rashes, and microbial resistance[5].

Furthermore for grades 1 and 2 acne, the topical side effects like flaking, dryness, burning, and itching, which can be uncomfortable and visibly noticeable, can potentially cause embarrassment and self-consciousness in social situations[18]. For grades 3 and 4 acne, treatment typically involves oral antibiotics such as doxycycline in combination with topical products. However, these treatments carry risks of side effects like itching, fatigue, rashes, gastrointestinal disturbances, and photosensitivity, as well as contributing to antimicrobial resistance[22].

The physical discomfort and concerns about antibiotic resistance can increase anxiety and affect adherence to treatment, further impacting patients' mental well-being, leading to psychological distress, including low self-esteem, social withdrawal, anxiety, and depression. Patients may avoid social interactions to prevent embarrassment or negative judgments, leading to isolation and a diminished quality of life, especially in adolescents[23]. Therefore interplay between the side effects of treatments and the psychosocial impact of acne underscores the need for therapeutic approaches that address both the physical and psychological aspects of the condition.

Phototherapy/Low-Level Laser Light Therapy

Thus, other alternative treatments are phototherapy (also known as photobiomodulation). The common uses of phototherapy are lasers (light amplification by stimulated emission of radiation) and LEDs (light emitting diodes). These lasers work since the bacterium of cutibacterium acne produces porphyrins[24]. The porphyrins can absorb light energy in the blue and ultraviolet light spectrum. Once that light is absorbed, there is a production of singlet oxygen, which, over time, helps eliminate the bacterium and treat the acne.

Various studies have been conducted using blue light treatment for acne. One specific study contained 89 people in hemiface; half used blue light therapy.The blue light therapy was used twice a week for six weeks. It was effective in treating hemifacial compared to untreated hemiface, as there was a 40% reduction in inflammatory acne lesions[25].

In another study, 30 people were treated with blue light therapy eight times, twice a week. Another thirty people were treated with 5% Benzoyl Peroxide, a topical treatment that was self-applied twice daily, every day during the time frame. The results showed that blue light therapy was equivalent to benzoyl peroxide in treating acne; however, a benefit of blue light therapy was the decrease in side effects of topical products of benzoyl peroxide. The use of blue light after three weeks showed a significant decrease in inflammatory lesions and erythema, making the skin smoother and having a better tone[24].

For grade 1 and grade 2 acne, the use of blue light therapy would not be a significant improvement to standard treatments of antibiotics. However, for the more severe cases of grade 3 and grade 4 acne; then, it would be considered a safe alternative to

combat possible antibiotic resistance. This process has recently been used for inflammatory acne with red light. Where the use of red light helps reduce pain and inflammation while also improving the repair process of tissues and regenerating other nerves. The biological process behind this low-level laser therapy (LLLT) is through light absorption through mitochondrial chromophores. Once absorbed, it is contained in the respiratory chain, where a series of events occur, leading to an oxidation state, improving ATP production in the mitochondria. More ATP can help fuel other cell processes, such as tissue repair and regeneration.

Consistent with these observations, previous studies have indicated that red light therapy can enhance cellular function and promote healing by stimulating mitochondrial activity, leading to increased ATP production and cellular proliferation[26]. This mechanism underscores the therapeutic effects of LLT in various dermatological conditions, including acne, wound healing, and skin rejuvenation.

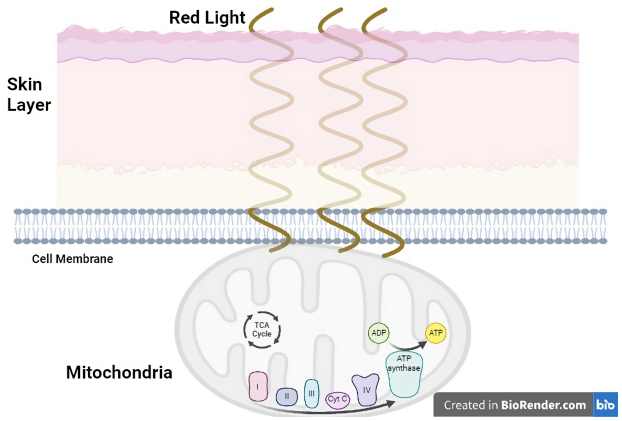

Fig. 2 Following the absorption of red light passing through the cell membrane, the mitochondria's production of ATP increases[27].

In addition LLLT increases the collagen production while decreasing collagen degradation by increasing the production of fibroblast and increasing PDGF effects which stimulates new gene expression as shown in Figure 3[27]

For acne, LLLT works by involving hypercornification, increased sebum secretion by hormones, and colonization of Propionibacterium acnes, and inflammation2. Thus in Figure 4 a swollen pore forms through bacteria spreading from the sebaceous gland.

However, there are still concerns about using LLLT, which is how exactly the molecular and cellular mechanisms translate signals from photons to the cells for the biological effects. Also, there can be significant variations in wavelength, power density, energy, irradiation time, and many more that can result in less effective treatments and damage the tissue instead of aiding it[27]. It should then come to mind to use the appropriate variations to best optimally use LLT on patients. The wavelengths generally

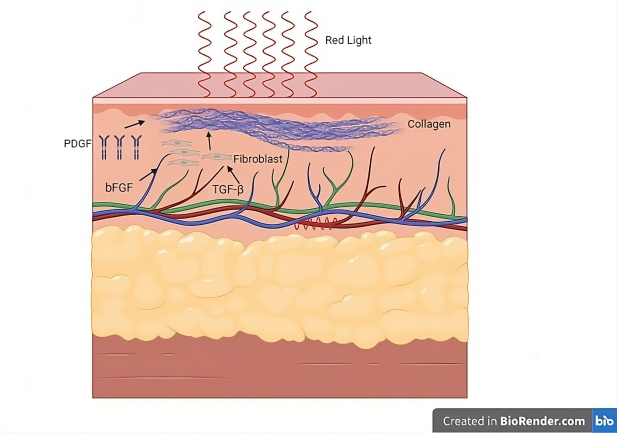

Fig. 3 As red light is absorbed in the skin it increases the effects of PDGF and Fibroblast production by decreasing apoptosis through TGF-β and bFGF. Thus collagen production is increased and collagen degradation is decreased[27].

used are between 3390 nm to 1,100 nm range. The lesser ranges, such as 390 nm to 600 nm, are used to treat superficial tissues, while the longer wavelengths, such as 600 nm to 1000 nm, are used to treat deeper tissues. It has been noted, though, that the range of 700 nm to 750 nm has been discovered to lack biochemical activity compared to other wavelengths, causing it to be rarely used[27]. Still there are laser devices such as the 1450-nm Diode Laser which was reported to have adverse effects of erythema which is the redness of the skin and swelling[28].

Additionally, there is no exact answer to the comparison of coherent lights compared to LED lights, as coherent lights are used to treat deeper tissues, while dermatologists commonly use LEDs to treat more extensive areas of tissue that need irradiation. With a pulsed light which uses light ranging from 500 to 1200 nm had effects limited to erythema, tingling, and burning. Thus, although effective with inflammatory acne, laser therapy has been associated with erythema, phototoxicity, pustular eruptions-rashes filled with inflammatory cells-, and epithelial exfoliation -peeling of epithelial cells which include skin cells[28].

However, LLLT comes in to serve as a popular alternative therapy to treat acne because of the unwanted side effects from topical treatments and slower results for antibiotics due to resistance. Blue light is better at repairing tissues for skin inflammation, as when the acne absorbs the blue light, it creates a reaction that forms free radicals and singlet oxygen species that turn into bacterial destruction[27]. Red light still affects sebum secretion and the released cytokines from before to reduce the inflammation, thus both having beneficial effects. In turn, red light and blue light treatments can help halt the sebum secretion in the sebaceous gland, as shown in Figure 5.

These results align with previous research suggesting that low-level laser light therapy (LLLT) is an effective alternative for managing skin inflammation, particularly in cases where

traditional treatments, such as antibiotics, face limitations due to resistance or side effects. As noted in studies by Avci et al. (2013), LLLT can stimulate tissue repair, collagen production, and reduce sebum secretion, which addresses multiple underlying causes of acne and skin inflammation. This supports the idea that integrating LLLT with psychological therapies, such as biofeedback, enhances the treatment of stress-induced skin conditions.

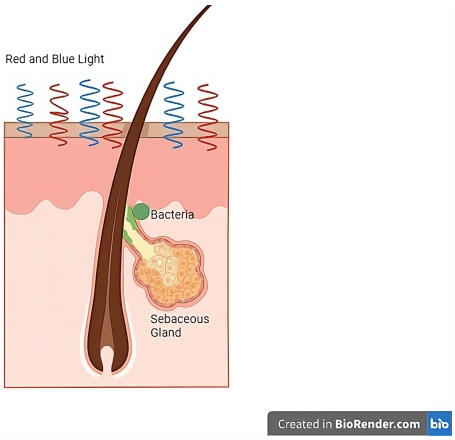

Fig. 4 Red light affects the sebum secretion reducing the inflammation while the blue light creates free radicals that turn into bacterial destruction[27].

Biofeedback Therapy and Acne Severity

As with other dermatologic treatments, biofeedback-assisted relaxation imagery therapy can further reduce acne. Biofeedback is a technique that involves monitoring physiological processes such as heart rate, muscle tension, skin temperature, and brain wave patterns. This is gathered from sensors attached to the body to detect these signals, which are then displayed on a screen that allows immediate feedback for individuals to become aware of their physiological state and adjust them consciously. Relaxation imagery is a therapy that can help adjust that feedback by using guided imagery and visualization techniques to evoke calming and peaceful mental images such as a meditation imagining a beach. This practice then can reduce stress and trigger relaxation responses in the body such as lowering muscle tension. A study found that relaxation imagery significantly reduces acne severity compared to other medical control treatments[29]. Now, it has to be determined whether these acne reductions are statistically significant for clinical dermatologists. The treatment group used in combination with biofeedback therapy,lesion extraction and medication while the control group had used only lesion extraction and medication to treat acne[29]. With the 14-week follow-up period, there was a statistically significant reduction in acne across the treatment group, meaning that there was 1.0 grade point reduction in acne severity measured from the acne grading scale which may reflect a 30-50% (p=0.001)[29] reduction in lesion counts according to the global acne grading system. For example, someone with moderately severe acne who is considered grade 3 improved to moderate acne which is grade 2.

These findings highlight the potential of psychological interventions, specifically biofeedback-assisted relaxation imagery, in improving skin conditions by directly targeting stress-related physiological responses. By teaching patients to control stress-induced physiological arousal, biofeedback therapy can reduce the activation of the HPA axis and decrease cortisol levels, leading to reduced inflammation and acne severity[30]. Moreover, empowering patients with self-regulation techniques enhances their sense of control over their condition, which can improve adherence to treatment and overall quality of life[17].

However, there was no significant clinical improvement in acne in patients receiving a 14-week follow up with standard dermatologic treatments with patients having been receiving clinical treatment a year before. Thus, only mild improvements were recorded. Compared to other treatments, the use of biofeedback-assisted relaxation imagery is proven to be effective[29].

To assess stress level in participants, electromyographic readings were recorded to measure muscle tension. Electromyography is a technique that uses sensors placed on the skin to detect electrical signals produced by muscles when they contract. Muscle tension is used as a physical sign of stress that can be felt as stiffness or tightness in the muscles. It was found that low levels of muscle tension while engaged in controlled relaxation, such as the imagery from the biofeedback therapy, was supported to decrease the acne severity[29]. Before the results, it was hypothesized that acne would be reduced if patients were interrupted and their stressful activities decreased. However, group subjects who frequently used muscular relaxation showed positive improvements in their acne with the use of positive imagery and muscle relaxation[29]. The subjects who participated in the relaxation imagery had no change in treatment; however, they showed increased confidence and small personality shifts that potentially affected the group's respective treatment.

It is also to be noted that the patients before the treatment had expected a moderate to significant improvement in their acne condition for the treatment they would receive. During the post-treatment phase of the study, the patients commented that their acne had improved just a moderate amount compared to the moderate to significant improvement[29]. However, not all the changes in acne severity were moderate, as they differed between subjects in the relaxation imagery group, with their improvement becoming more significant. In other comparison groups, the perceived moderate degree was inaccurate compared to the imagery group[29]. Though biofeedback-assisted relaxation and guided cognitive imagery are effective treatments for further reducing acne for those already using traditional dermatologic medicine, there are still limitations to consider.

Effective biofeedback therapy typically needs assistance from trained professionals thus therapy sessions can be expensive and inaccessible for some individuals. As significant results often require multiple sessions over an extended period of time and the effectiveness varies from person to person with the specific condition of stress or anxiety a person may have[31].

Despite these limitations, incorporating accessible stress-reduction techniques into daily routines can offer benefits. Even everyday physical activity is well established to reduce stress and can be effective in reducing stress-related symptoms[32]. Activities that focus on positive characteristics, such as music therapy, yoga, and meditation, can also mitigate stress[14].

The findings on biofeedback-assisted relaxation imagery align with previous research that emphasizes the mind-body connection in dermatology. Stress-induced activation of the hypothalamic-pituitary-adrenal (HPA) axis, as highlighted by Peters (2016), plays a significant role in skin inflammation. By reducing stress through biofeedback techniques, patients can decrease physiological stress responses, which in turn reduces the severity of skin conditions such as acne. The combination of LLLT and biofeedback not only reduces microbial and inflammatory factors but also addresses the psychological stressors that exacerbate these conditions, creating a more holistic approach to treatment.

Discussion

The result of the study showcased that the use of low-level laser light therapy provides a positive correlation in decreasing skin inflammation, such as acne, by restoring the wound healing process. These findings are consistent with existing literature that highlight LLLT's role in enhancing skin repair mechanisms and reducing inflammatory responses. In combination with relaxed biofeedback therapy can be beneficial to provide less acne severity to patients.

These findings raise the question on how effective is the combined use of low-level laser light therapy (LLLT) and biofeedback therapy in mitigating stress-induced skin inflammation of acne compared to traditional treatments, and what are the underlying mechanisms through which this integrated approach influences the hypothalamic-pituitary-adrenal (HPA) axis and skin immune responses?

However, several limitations in the current research warrant further investigation. Firstly, there is a need for comprehensive studies examining the combined effect of LLLT and biofeedback therapy on skin inflammation. Future research should focus on randomized controlled trials with larger sample sizes to determine the efficacy and safety of this combined approach. Such studies could provide more specific results and help establish standardized treatment protocols.

Secondly, potential biases favoring LLLT over oral antibiotics, or the limited amount of research on biofeedback therapy in relation to skin inflammation like acne, should be addressed. Future studies should include comparative analyses between these therapies and traditional treatments to evaluate their relative effectiveness and identify any synergistic effects.

Moreover, exploring the individual differences in stress perception and their impact on skin conditions could contribute to personalized treatment strategies. Investigating how varying levels of chronic stress influence the severity of skin inflammation may help tailor interventions to individual patient needs.

Another area for future research is understanding the underlying mechanisms by which psychological stress exacerbates skin inflammation. Further studies on the role of cytokine profiles, neuroendocrine factors, and immune system modulation in stress-induced skin conditions could provide insights into novel therapeutic targets.

Lastly, the long-term effects and sustainability of combining psychological and physical therapies need to be evaluated. Longitudinal studies assessing patient outcomes over extended periods would help determine the lasting benefits and potential limitations of these integrated treatment approaches.

In conclusion, while integrating psychological and physical therapies offers a promising avenue for treating stress-induced skin inflammation, further research is essential to validate these findings and develop evidence-based guidelines. Advancing our understanding in this area could lead to improved patient outcomes and contribute to a more holistic approach in dermatological care.

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