Photodiagnosis and Photodynamic Therapy 14 (2016) 191–199

Contents lists available at ScienceDirect

Photodiagnosis and Photodynamic Therapy

journal homepage: www.elsevier.com/locate/pdpdt

Review

Photodynamic therapy for the treatment of different severity of acne: A systematic review

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ARTICLE INFO

Article history:
Received 19 January 2016
Received in revised form 31 March 2016
Accepted 10 April 2016
Available online 16 April 2016

Keywords:
Photodynamic therapy
Acne vulgaris
Light source
Photosensitizing agents

ABSTRACT

Introduction: Acne, a disease of pilosebaceous unit, is a common dermatologic disorder affecting about 80%–95% of people in both genders in adulthood. The available treatment options are conventional topical and/or oral medications, which are associated with adverse effects, partial response only, contraindications and reoccurrences. This necessitates the need for the introduction of novel treatment for improving acne lesions.

Objective: The aim of writing this review is to provide evidence-based information regarding safety and efficacy of PDT in treating acne lesions.

Method: The search term 'Acne and PDT' were entered into a search of the National Library of Medicine's PubMed Database. The search returned a total of 143 sources among which 36 studies pertaining to the use of PDT in acne are included in this review article.

Result: 36 clinical trials were selected among which 24 trials were performed to see the effect of PDT in acne whereas 12 trials compared the effect of PDT with light or laser alone therapy. Among 24 trials that used PDT only, 3 were clinical trials with control, 14 were clinical trials without control, 6 were randomized controlled trials (RCT) and 1 was retrospective study. On the basis of results of these trials, it is seen that PDT is safe and effective method of treatment for acne lesions. Studies have shown that PDT can control both inflammatory and non-inflammatory acne lesions and can improve all severity of lesions from mild to severe.

Conclusion: Photodynamic therapy (PDT) has been extensively studied and found to be effective treatment modality for acne lesions. However, more RCTs are needed to establish standard guidelines regarding concentrations and incubation period of photosensitizers and optimal parameters of light sources. Further studies are needed to guide future research and help dermatologist to choose PDT as an effective treatment modality for treating acne lesions.

Contents

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http://dx.doi.org/10.1016/j.pdpdt.2016.04.005
1572-1000/

1. Introduction

Acne vulgaris (or simply acne) is a common skin condition that affects people of all races and all ages. It is basically an inflammatory disease of pilosebaceous unit, which is composed of sebaceous gland, a hair follicle and a hair shaft [1]. Acne lesions appear primarily on the areas with high concentration of sebaceous glands such as face, back and chest. Sebaceous glands secret sebum, which consists of fatty acids that support the colonization by *Propionibacterium acnes*, the bacterium associated with acne [2]. Acne has diverse clinical presentations, which include seborrhea (excess production of a greasy secretion), non-inflammatory lesions (open and closed comedones), inflammatory lesions (papules and pustules), post inflammatory hyperpigmentation, and variable degrees of disfiguring scars [3]. Moreover, moderate to severe acne may have negative impact on psychological wellbeing and quality of life. Conventional therapies for acne include topical therapies such as antibiotics, benzoyl peroxide, and retinoids, and systemic therapies such as antibiotics, hormonal agents, and oral retinoids [4,5].

They are believed to work in at least four different ways including, anti-inflammatory effects, hormonal manipulation, killing *P. acnes*, and normalizing skin cell shedding and sebum production in the pore to prevent blockage [6]. Due to the reason that antibiotic resistance and adverse treatment profiles can complicate these therapies, an alternative treatment modality is needed. PDT is among one of the extensively studied optical treatment that has shown to be safe and effective in treating acne lesions.

PDT is a non-invasive therapy that utilizes light treatments along with an application of a photosensitizing agent (PA). The common photosensitizing agents used in PDT for acne are 5-aminolevulinic acid (ALA) and methyl aminolevulinate (MAL). Recently, indole-3-acetic acid (IAA) has been introduced as a new photosensitizer. It is hypothesized that once applied to the skin, photosensitizing agents are preferentially taken up by the pilosebaceous unit and augment the response to light therapy. PDT light sources include laser, intense pulsed light, light-emitting diodes (LEDs), blue light, red light, and many other visible lights including natural sunlight. The photosensitizing agent is applied to the skin, causing the skin to become more susceptible, or receptive, to light. After the photosensitizing agent is removed, a light treatment is administered. Various light therapy alone have also found to improve acne, especially blue light due to its anti-inflammatory effects [7–12]. However, it was seen that acne clearing was variable among patients and relapse rates were high after therapy was discontinued [13–16]. Also due to the reason that the effects of all light-alone treatments are temporary and appear to apply only to mild to moderate acne, its use is limited.

2. Method

A systematic review of the literature was performed on December 15, 2015 to find articles relevant to the treatment of acne with PDT. The search term 'Acne and PDT' was entered into a search of the National Library of Medicine's PubMed Database. The search returned a total of 143 sources. All the original articles pertaining to the use of PDT in acne were selected. This selection yield a total of 36 clinical trials among which 24 trials were performed to see the effect of PDT in acne and 12 trials were comparative studies that compared the effect of PDT with light or laser alone therapy. Among the 24 trials that used PDT only, 3 were clinical trials with control, 14 were clinical trials without control, 6 were randomized controlled trials (RCT) and 1 was retrospective study. Remaining 107 out of 143 studies were excluded because they were either review articles or they used PDT in treating conditions other than acne vulgaris.

2.1. Clinical trials with control

Our search identified 3 clinical trials with control [17–19]. All the three trials used topical ALA as a photosensitizer. Regarding light source, Alexiades-Armenakas et al. [17] used long pulsed pulse dye laser 595 nm, 7.0–7.5 J/cm^2 fluence, 10-ms pulse duration, 10-mm spot size, and dynamic cooling spray of 30 ms with a 30-ms delay, Gui-Lan Yang et al. [18] used red light 633 ± 10 nm, 100 mW/cm^2, 50 J/cm^2 for 20 min using a light irradiation apparatus with a LED-IB lamp, Hong et al. [19] used red light at 630 ± 63 nm using a halogen light source demonstrating energy-density uniformity within an irradiated field of 69 cm^2 for 10 min, energy intensity and total energy of 30 mW/cm^2 and 18 J/cm^2. All the three trials showed better effect in the treatment group comparing to the control group. Complete clearance was achieved in 100% patients [17], response rate of 100% was seen [18] in treated group and the mean percentage reduction in inflamed lesions at 1, 3 and 6 months was 27.6%, 37.9%, and 41.9% respectively in the treated area, whereas in the control area it was 8.0%, 14.7% and 15.4% respectively compared with the baseline [19]. Adverse effects were localized, transient or mild for these clinical trials. More importantly, one study [17] has shown PDT to be effective in all skin types including Fitzpatrick skin types I–VI.

2.2. Clinical trials without control

Our search identified 14 clinical trials without control [20–33]. The photosensitizers that were used in these trials are topical ALA 5% to 15% in gel, cream or lotion preparation [20,22,24–26,28,29,31–33], oral ALA 10 mg/kg body weight [23], 0.5% ALA spray [27], topical IAA [21], and topical MAL 80 mg/g [30]. The light sources used were red and green light source with three panels containing halide lamps [20], green light [21], LED light [22,25,28], polychromatic visible light from metal halide lamp [23], polychromatic visible light by halogen light source [26], blue light [24], IPL [27,33], red light [29–31], and advanced fluorescence technology (AFT) pulsed light source [32]. The studies did not mention how they choose the dose of photosensitizing agent and parameters of light source. However, in one study [29], to examine the time course of protoporphyrinIX (PpIX) production, 10% ALA was applied to inflammatory papules for 1–5 h and followed by in situ fluorescence examination and to determine the effects of ALA dose and lesion type, 3, 5, and 10% ALA was applied to acne lesions in split-face fashion for 3 h followed by whole-face light irradiation at 633 nm and 30–70 J/cm^2 and found that PpIX reached a stable level after 3 h of incubation. Similar PpIX levels were seen in areas receiving 3, 5, and 10% ALA. Poisson regression analyses indicated that lesion counts decreased by 0.791 times for a one-unit increase in treatment times but only by 0.999 times for a one-unit increase in ALA dose.

The sessions of PDT varied from 2 to 5 sessions in majority of studies but in one study [26], only single session of PDT was delivered and all the 13 patients treated had apparent improvement of facial appearance and reduction of new acne lesions at 1, 3 and 6 months following PDT treatment. However, this study had longer incubation period (4 h) and higher concentration (20%) of ALA comparing to other studies where incubation period varies from 15 min to 90 min and concentration of ALA varies from 0.5% to 10%. This may be the reason for multiple adverse effects seen in this study, which were either not seen in other studies or if seen, were milder and transient. The adverse effects were discomfort, burning and stinging during irradiation, oedematous erythema for 3 days after PDT, epidermal exfoliation from the fourth to the 10th day, irritation and hypersensitivity to physical stimulation for 10 days after PDT, and pigmentation or erythema after epidermal exfoliation; the treated lesions returned to normal skin conditions within 1 month.