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Review Article

PHOTODYNAMIC THERAPY FOR THE TREATMENT OF ACNE –A REVIEW

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ABSTRACT

Acne is the most common disease we can find in the dermatology that has brought physical and psychological burden in many patients. Previously, the treatment was bound to only systemic, topical antibiotics and retinoid. Now, many light therapies are playing vital role in the treatment of acne, mostly photodynamic therapy. Photodynamic therapy is a recently emerging treatment for acne in which with the help of light activation the cells are destroyed by photosensitizers applied in the skin to produce reactive oxygen species with minimal side effects.

Keywords: Acne, photodynamic therapy, aminolevulinic acid, light sources

INTRODUCTION

Acne vulgaris is a chronic inflammatory pilosebaceous follicle disease, characterized by comedones, papules, pustules, nodules and sometimes scars. It is found in about 80% of young adults and adolescents. In recent years, acne is seen in young patient due to earlier onset of puberty. A systemic analysis for Global Burden of Disease study indicated that acne was the 8th most prevalent disease worldwide in 2010[1].The pathogenesis is multifactorial and includes [2]:

1. Inflammatory
2. Excess sebum production
3. Obstruction of pilosebaceous unit
4. Irregular follicular desquamation

The main microorganism involved for acne is Propionibacterium acnes. P.acnes induce inflammation in the skin by activating Toll-like receptor TLR-2 and TLR-4, which in turn trigger the production of inflammatory cytokines such as interlukin IL-1, IL-8, IL-12[3].

Different methods are introduced by different individuals, as Burke, Cunliffe and Gibson introduced the Leeds technique in 1984, Doshi ,Zaheer and Stiller presented global acne grading system(GAGS) in 1997, Hayashi et al., used standard photography in 2008 and many more, for measuring the severity of acne among which the most popular is grading and counting lesions. The earliest was published by Pillsbury,Shelly and Kligman in 1956 as[4,5];

- Grade 1: few or a lot of comedones with little or no inflammation
- Grade 2: comedones and small superficial pustules and inflammatory lesions in the follicle
- Grade 3: comedones, small and large inflammatory papules and pustules with more extensive
- Grade 4: comedones and deep confluent lesions with canalized sinus

Various treatment modalities for acne have been formulated according to the stage and intensity of disease which includes use of topical, systemic, complementary and alternative medicines, physical treatment [6].

Treatment modalities for acne:

1. Topical treatment:
   a. Antibiotics(Benzoyl peroxide, Clindamycin, Azelaic acid, Dapsone, Erythromycin)
   b. Retinoids (Adapalene, Tazaroten, Tretinoin)
   c. Combination medication(antibiotics + retinoids)
2. Systemic treatment:

a. Oral antibiotics(Doxycycline, Tetracycline, Minocycline, Azithromycin)
b. Hormonal treatment(Spironolactone, Prednisolone, Dexamethasone)
c. Oral retinoid(Isotretinoin)

3. Other treatments: Resurfacing, Dermabrasion, Laser resurfacing, Chemical peels, Xenografts, Fat transplantation [7].

Topical antibiotics are commonly used in the treatment of mild to moderate acne. However, the problem of antibiotics resistance caused by topical antibiotics, especially macrolides has become increasingly worrisome. Due to the significant decline in the clinical efficacy of topical antibiotics the use of oral antibiotics are increasing in the recent years which is also leading to the resistance. The gradual resistance to antibiotics is recently decreasing the success rate of topical and systemic antibiotics which were the mainstay treatment for acne. Researchers showed that more than 50% of P. acne is resistant, especially macrolides [8]. Therefore, the safer and effective modalities of treatment have been developed. In the recent years, light therapies such as Photodynamic Therapy has been playing major role in dermatological practice. It is indicated for the treatment of Non-melanoma skin cancer, actinic keratosis lesions, Basal cell carcinoma, Bowen's disease, Photoaging.

History of PDT:

In 20th century, Munich, Oscar Raab and Herman Von Toppeiner were the first to develop PDT when they noticed the effects of photosensitivity on paramecia. Later Von Toppeiner discovered that there is need of oxygen for the reaction to occur. In earlier 1960s, a new drugs based on the purification of hematoporphyrin Hp was synthesized called hematoporphyrin derivative (Hpd). Due to the lack of publication in medical literature dermatological technique was hindered until 1990[9]. Later, a new method using topical Aminolevulinic Acid (ALA) as a metabolic precursor of the endogenous photosensitizer, protoporphyrin IX (PDIX) was proposed by Kennedy et al. For the treatment of acne, Hongcharu and colleageus were the first to use PDT in the year 2000, USA.

It is hypothesized that PDT helps in reducing P.acne level and pilosebaceous unit size and function [2]. The 3 important factors in PDT are photosensitizers, light and oxygen. Photosensitizers in PDT involve systemic photosensitizers, topical photosensitizers and light sources. The most commonly used photosensitizers are protoporphyrin IX (PpIX) precursor 5-Aminolevulinic acid or Methyl aminolevulinate (MAL) with a laser or broad band light sources. 5-ALA photodynamic therapy has been approved abroad for the treatment of actinic keratosis and dermatitis. Domestic and foreign scholars have systematically studied the mechanism of ALA PDT in the treatment of acne and found thatit can effectively inhibit the secretion of sebaceous gland, inhibit the keratinized epithelial cells of hair follicles and kill the pathogenic microbes in the hair follicles which are the cause of acne [10] . The main mechanism of action is summarized below:

Photodynamic therapy → Pilosebaceous unit → Light sources → Porphyrin(Coproporphyrin III, Protoporphyrin IX) → light wavelength 400-700nm → photo-excitation of porphyrins by heme biosynthetic pathway → release of singlet oxygen and reactive preradicals → bactericidal to P. acne

The different light sources such as Intense Pulsed Light (IPL), Light Emitting Diodes (LEDS), Fluorescent Lamp, and Pulsed Dye Laser (PDL) are used to activate Protoporphyrin IX. Photodynamic therapy absorbed by pilosebaceous unit is activated by these light sources which lead to the photo excitation of protoporphyrin IX by heme biosynthetic pathways. These precursors accumulate into the sebaceous glands on the skin and are incorporated into heme synthesis pathway to produce increased amount of PpIX. Then the visible spectrum of light is exposed in the presence of oxygen to activate photosensitizers that generate reactive oxygen species and induce selective phototoxicity of the targeted sebaceous units. Thus , ALA-PDT help in the treatment of acne by photodynamic injury of sebaceous gland, killing of Propionibacterium acnes and reduction of follicular obstruction through changing keratinocytes shedding and hyperkeratosis[11]. Among various different light sources Red light are used as the light sources because it can penetrates deeper in the tissue and target sebaceous gland.

There have been many studies done to evaluate the use of PDT for acne with different range of photosensitizer, light sources, time of frequency, and number of reaction. While many shows good results and demonstrate the useful therapy for acne by PDT. Some are listed below [12]:

Author	No. of patient	Photosensitizer	Light sources	Treatment session
Hongcharu, 2000	22	20% ALA	Broadband light	4session, every 1week
Horfelt, 2006	30	16% MAL	Red light	2session, every 2week
Chen et al. 2015	50	5% ALA	Infrared light	3sesssion, every week
Akaraphanth, 2007	20	10% ALA	Blue light	4session, 1week apart
Yew, 2016	15	5% ALA	Red light	1session
Taw, 2015	136	3.6% ALA	Red light	3session, every 2week
Asayama-kosaka, 2014	11	5% ALA	Broadband light	1 session
Yang, 2013	75	5% ALA	Red light	every 10days, 1month
Ying et al. 2010	180	5, 10, 15, 20% ALA, IPL	Red light	4session, 10days apart
Pariser et al. 2016	153	8% MAL	Red light	4session, every 2weeks

Above studies done in different years showed the most commonly use photosensitizer were ALA and MAL at different concentration (5, 10, 15, and 20%). The increasing in the strength of photosensitizers increases the clearance rate of acne but lead to more adverse effects. The adverse effects include erythema, edema, blisters, crust, purpura, post inflammatory hyperpigmentation which were found to be gradually subsiding after few weeks of treatment. Among the various light sources Red light and Blue light were used frequently to activate the photosensitizers in PDT. Red lights were found to penetrate deep in the dermis and target the sebaceous gland due to its larger wavelength. Generally, after applying photosensitizer the skin was occluded with the plastic film for 1-3hours and then the light was passed. This procedure showed successful reduction in acne lesions due to the better penetration. The numbers of PDT sessions depend on the patient's response to treatment. Evidence and research done previously supports that PDT therapy can improve acne lesions (mild-moderate inflammatory lesions) [12,13]. Hongcharu et al., in the year 2000 reported the number of inflammatory acne lesions and sebum secretion level were significantly reduced after 4 session of treatment. Ma et al. reported higher efficacy rate in severe cystic acne patients group compared to mild group [14].

CONCLUSION

However, due to lack of clinical studies, insufficient data dosing and number of treatment required, the studies have been limited. Several studies have found increased advantages of PDT. PDT has been studied and found to resolve acne faster and more effectively with fewer side effects in acne vulgaris. Thus, in future more research is needed, to establish standard guidelines for the use of PDT for the right patient at the right time.

REFERENCES

1. Moradi tuchayi, Sara & Makrantonaki, Eugenia & Ganceviciene, Ruta & Dessinioti, Clio & R. Feldman, Steven & Zouboulis, Christos. (2015). Acne Vulgaris. Nature Reviews Disease Primers. 1. 10.1038/nrdp.2015.29
2. Monica Boen, Joshua Brownell, Priyanka. Patel, Maria M. Tsoukas The role of photodynamic therapy in acne 2017-3-08 Am J Clin Dermatol DOI 10.1007/s40257-017-0255-3
3. Aydemir EH. Acne vulgaris. Turkish Archives of Pediatrics/Türk Pediatri Arşivi. 2014;49(1):13-16. doi:10.5152/tpa.2014.1943.
4. Adityan B, Kumari R, Thappa DM. Scoring systems in acne vulgaris. Indian J Dermatol Venereol Leprol 2009;75:323-6
5. Camilla Horfelt Photodynamic therapy for the treatment of acne vulgaris in clinical studies:dose response and mode of action 2009 ISBN 978-91-628-7579-4
6. Fox L, Csongradi C, Aucamp M, du Plessis J, Gerber M. Treatment Modalities for Acne. Molecules. 2016; 21(8):1063.
7. Amber Vyas, Avinesh Kumar Sonker, and Bina Gidwani, "Carrier-Based Drug Delivery System for Treatment of Acne," The Scientific World Journal, vol. 2014, Article ID 276260, 14 pages, 2014. https://doi.org/10.1155/2014/276260

8. Zhang Nanxue, LU Zhong, MA Ying, Current status of antibiotic treatment and drug resistance in acne 2018,(34)01,61-64
9. Issa, Maria Cláudia Almeida, & Manela-Azulay, Mônica. (2010). Photodynamic therapy: a review of the literature and image documentation. Anais Brasileiros de Dermatologia, 85(4), 501-511. https://dx.doi.org/10.1590/S0365-05962010000040001
10. Li qi xia, Gong yu shun, Zhao xiao hui, Mechanism of action of ALA-PDT treat for acne vulgaris.1672-7738(2009)06-0360-05
11. Megna M, Fabbrocini G, Marasca C, Monfrecola G. Photodynamic Therapy and Skin Appendage Disorders: A Review. Skin Appendage Disorders. 2017;2(3-4):166-176. doi:10.1159/000453273.
12. Rai R, Natarajan K. Laser and light based treatments of acne. Indian J Dermatol Venereol Leprol 2013;79:300-9
13. Pei S, Inamadar AC, Adya KA, Tsoukas MM. Light-based therapies in acne treatment. Indian Dermatol Online J 2015;6:145-57
14. Calvina Theresia, Jie Zheng, Xiao-Ying Chen,Topical ALA-PDT as alternative therapeutic option in treatment-recalcitrant dermatosis: Report of 4 cases,Photodiagnosis and Photodynamic Therapy,Volume 20,2017,Pages 189-192,ISSN 1572-1000,https://doi.org/10.1016/j.pdpdt.2017.10.010.