

PUVA THERAPY- A BOON IN DISGUISE FOR VARIOUS SKIN DISORDERS: A REVIEWTanha Khan¹, Upender Malik², M. K. Sunil³, Nayira Johar⁴PG student^{1,4}, Professor², Professor and Head⁴*1-6- Department of Public Health Dentistry, Teerthanker Mahaveer Dental College and Research Centre, Moradabad, Uttar Pradesh, India***Abstract**

Phototherapy is a technique which uses ultraviolet irradiation with or without exogenous photosensitizer. It can be administered in various ways including Photochemotherapy (PUVA), Broadband UVB and Narrowband UVB. PUVA is a combination of Psoralen (P) and long- wave ultraviolet radiation (UVA). This method is used for treatment of various dermatologic disorders. Although, there are few adverse effects of PUVA therapy, its use as treatment modality is increasing nowadays and the adverse effects can be reduced or avoided with careful monitoring of dosimetry of the administered radiation.

Keywords: Photochemotherapy, Psoralen, UVA

Introduction:

The electromagnetic spectrum contains various components, out of which UV radiation is a small component with a narrow band of radiation from 200-400 nm. Moreover, UV spectrum is divided further into 3 types of radiation based on the wavelength: UVC (200-280 nm), UVB (280- 315 nm) and UVA (315- 400 nm). The therapeutic use of UV radiation without exogenous photosensitizer is the basis of phototherapy. Phototherapy can be administered in various ways such as: Photochemotherapy (PUVA), Broadband UVB therapy and Narrowband UVB therapy, Excimer 308 nm laser treatment, UVA1, Photodynamic therapy.¹

One such therapeutic modality includes PUVA or Photochemotherapy. PUVA stands for Psoralen plus Ultraviolet A. Photochemotherapy or PUVA is the method for treatment in which therapeutic response is induced by using radiation of appropriate wavelength in the presence of photosensitizing drug. PUVA therapy use combination of Psoralen and longwave ultraviolet (UVA) radiation.^{2,3}

A target molecule is used in photochemotherapy which absorbs the radiation. A chromopher which is an

exogenous drug is used as a target molecule in photochemotherapy. In dermatology,

UV and visible radiation are used therapeutically: UVC is absorbed by ozone layer, UVB for phototherapy, UVA for photochemotherapy and visible light for photodynamic therapy. PUVA therapy have become nowadays a popular alternative to dermatologic therapy.^{4,5,6}

History of phototherapy:

The useful effect of sunlight was first recognized by the ancient Egyptians. The spectrum of visible light was discovered by Newton in 1672. UV light was first discovered in the year of 1700s. Modern phototherapy began in the year of 1895, when Niels Finsen who is also known as the Father of modern UV therapy treated Lupus vulgaris by using a carbon arc source. Because of this, he was also awarded the Nobel Prize in 1903. Various uses of UV radiation were introduced for treating many skin disorders at that time. Goeckerman used the combination of artificial UVB along with coal tar for treating psoriasis in the year 1923. Ingram, in 1953, introduced the combination of artificial UVB and dithranol. It was then believed that UVB on its own is

very effective for treating dermatological disorders. Then in 1984, Van Weelden showed that narrowband UVB was also efficacious. It was then proven that narrowband UVB was more effective as dermatological therapy as compared to broadband UVB.¹

History of photochemotherapy:

Since ancient times, as early as 1500 BC, photochemotherapy was used for the treatment of vitiligo by using extracts of plants and subsequent exposure to sunlight, in India and Egypt. The first scientific use of photochemotherapy was done back in 1948 AD by Fahmy et al in the university of Cairo when they isolated three chemical compounds from the fruit of the plant Ammi Majus. These three components were named as Ammoidin, Ammidin and Majudlin.⁷ The role of psoralens photochemotherapy was then reported in 1953 by Lerner for treating patients with vitiligo.⁸ Parrish et al in 1974 reported the use of 8-methoxypsoralen (P) with UVA for the treatment of severe psoriasis and coined the acronym PUVA. The modern form of photochemotherapy with the help of high intensity UV- A sources was first introduced at Harvard- Massachusetts General Hospital Dermatology Laboratories.⁹

Administration of phototherapy:

It can be done in various ways-

- Photochemotherapy PUVA
- Broadband UVB therapy
- Narrowband UVB therapy
- Excimer 308nm laser treatment
- UVA1
- Photodynamic therapy

PUVA and Narrowband UVB therapy are most commonly used for treating various dermatological problems in India.¹

Chemistry of Photochemotherapy:

Psoralen are naturally present in some of the plant species and they belong to Furocoumarin class of compounds which are derived from fusion of Furan with a Coumarin. It is found naturally in many plants such as limes, lemons and parsnips. Psoralens include 8- MOPs (methoxysalens), 5- MOPs (Bergapten) and ^{4,5,8} TMPs (trioxsalen). Among the psoralens, trimethyl derivative is synthesized in vitro and not found naturally. Psoralens exhibit normal reactions of lactone of coumarin to give coumarinic acid or coumaric acid derivative. 7H- furo[3,2-g] chromen-7-one is the IUPAC name for psoralens.^{2,3,10}

Mechanism of action:

The wavelength of action of PUVA ranges between 320 and 400nm. Photochemotherapy includes 2 types of reactions which causes photosensitivity. One is anoxic reaction while the other is oxygen dependant reaction. Anoxic reaction affects cellular DNA and forms photo adducts and thus inhibiting the proliferation of epidermal cells causing apoptosis. And the other one, oxygen dependant reaction produces free radicals and reactive oxygen which damages membrane by lipid per oxidation. PUVA therapy induces melanogenesis in normal skin by transferring melanosomes from melanocytes to epidermal cells, resulting in increased pigmentation. PUVA acts on actively dividing cells rather than on resting cells. This is the reason why PUVA therapy is more effective on active state of skin diseases than their fibrotic state.^{2,6,11-15}

PUVA therapy in dentistry:

1. Psoriasis

PUVA therapy is most commonly indicated in Psoriasis. UVB is also commonly used for the treatment of

psoriasis. The efficacy of PUVA is more than e UVB but is similar to narrowband UVB. PUVA therapy is basically used in the cases where UVB cannot produce adequate results and cannot clear psoriasis adequately.²

Conditions in which PUVA is used instead of UVB-

- If UVB is not effective.
- If the duration of remission following 3 consecutive UVB sessions is shorter than 2 months.
- For palmoplantar psoriasis.

Method-

Crystalline 8-MOP is dissolved in the solution of 95% ethanol making it a 0.5% (w/v) stock solution. Then the final solution is made by diluting it with 100 litres of body temperature bath water making the final concentration of the solution as 0.0003% (w/v). The body surface is then soaked in this bath solution for 30 minutes, then quickly wiped dry. After that the patients are irradiated.²

2. Lichen planus

Psoralens are also used in the treatment of Lichen planus. UV irradiation along with psoralens has become an effective treatment method for lichen planus. It is seen that UVA light exposure of patients with Oral Lichen Planus lesions who have already been treated with psoralens have great therapeutic effects.²

3. Cutaneous T cell lymphoma

If treatment with topical steroids remain unhelpful, then PUVA proves to be a beneficial treatment modality. PUVA therapy can be given along with other therapies including retinoids or interferon. In patch stage disease, narrowband UVB is beneficial while in thickened and palpable lesions, PUVA therapy is much more effective.²

Indications:

PUVA therapy is effective in various cutaneous diseases such as:

- Psoriasis- specially in cases where more than 20% of body surface is involved.
- Cutaneous T-cell lymphoma
- Vitiligo
- Lichen planus
- Morphea
- Chronic graft vs host disease
- Dermatitis herpetiformis
- Mycosis fungoides
- Prurigo nodularis
- Granuloma annulare
- Photodermatoses
- Eczema
- Urticaria^{2,6}

Risks:

There are certain risks associated with PUVA therapy. They can be of acute as well as chronic types. Acute side effects which can occur includes erythema- similar to sunburn which in turn can form bullous lesions. Other risks includes pruritus, nausea. All these can be prevented by careful assessment of doses. Apart from this acute toxicity, there are several chronic toxicity. They are known to have carcinogenic and mutagenic effects. Hyperpigmentation and mottling are said to be another risks involved during PUVA therapy. There are various reports suggesting that patients undergoing PUVA therapy have increased risk of premature ageing of skin, actinic keratoses, epidermal dystrophy, skin cancer and Bowen's disease.^{16,17}

Contraindications:

- Pregnancy and lactation
- Severe liver disease
- Renal failure
- Xeroderma pigmentosum
- Systemic Lupus Erythematosus
- Family history of melanoma
- Generalized unstable psoriasis^{2,3,6}

Patient education:

It is the need to explain the entire procedure of PUVA therapy to the patients before starting the therapy. PowerPoint slides can be used for this purpose. Pre-treatment and post-treatment photographs can be shown to the patients where possible. It is advisable to discuss all sorts of adverse effects with the patients.⁶

Advantages:

Since certain skin diseases are characterized by rapid epidermal cell replication, PUVA proves to be beneficial in such conditions as this therapy is capable of inhibiting epidermal DNS synthesis. So basically, PUVA therapy shows efficacy in approximately 90% of patients with skin disorders such as psoriasis. It also proves to be cost-effective in patients with more severe skin disorders who would otherwise require hospitalization for treatment with other modalities.^{6,18}

Disadvantages:

Apart from various adverse effects, there are certain disadvantages of PUVA therapy, which are as follows- Technique using PUVA therapy such as bath PUVA needs longer session as well as extra supervision. In bath PUVA technique, after soaking is done in the

psoralen solution, exposure to UVA should be done immediately. This is because of the fact that photosensitivity declines rapidly. There is another technique where PUVA therapy is used known as Bathing suit PUVA. The main disadvantage of this technique is that, the entire body surface may not come in contact of the bathing suit. The another thing is that there may not be uniformity of concentration of psoralen in the bathing suit.⁶

Post-treatment skincare:

It is advisable to take proper care of the skin after phototherapy. PUVA therapy can cause the skin to become more sensitive to light and that is why patients undergoing PUVA therapy are more likely to get sunburn easily. Patients are advised to avoid direct sunlight as well as indirect sunlight even through window glass for 24 hours after treatment with PUVA. They are said to apply sunscreen with SPF 15 or more for at least about 24 hours after PUVA session. Scrubbing of the skin should be avoided to reduce the risk of trauma as any skin breaching can worsen the already existing skin disorder such as psoriasis. Patients are also said to avoid using perfume or colognes to the skin receiving PUVA as these materials can be photosensitizing and may increase the risk of burning during PUVA therapy. Moreover, sunbathing should be avoided during ongoing PUVA treatment, to reduce any risk of sunburn.⁵

Conclusion:

PUVA therapy is very efficient in treating various immunological disorders and systemic diseases such as psoriasis where a topical therapy alone does not prove to be that effective. PUVA therapy can also be administered in patients who have failed UVB therapy. When administered and monitored properly, PUVA can help patients to achieve clearance. For safety, doses of PUVA should be lower by changing the dose schedule and reducing unnecessary maintaining dose. It should be avoided in patients with history of skin cancer to

avoid any kind of recurrence. Thus, PUVA therapy proves to be a highly effective modality useful to treat various skin disorders with certain side effects, which can be very well reduced if administered properly.

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