

Targeted phototherapy

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ABSTRACT

Background: Targeted phototherapy is a new form of phototherapy which has many advantages and disadvantages over conventional phototherapy. This article reviews the different technologies and outlines recommendations based on current evidence. **Methods:** A literature search was performed on targeted phototherapy to collect data. Relevant literature published till March 2014 was obtained from PubMed, EMBASE, and the Cochrane Library. Keywords like “targeted phototherapy”, “excimer laser”, “excimer lamp”, “Nonchromatic ultraviolet light”, “vitiligo”, and “psoriasis”, were used for literature search. All systematic reviews, meta-analysis, national guidelines, randomized controlled trials (RCT), prospective open label studies and retrospective case series in English were reviewed. **Results:** Three hundred and forty studies were evaluated, 24 of which fulfilled the criteria for inclusion in the guidelines. **Conclusions and Recommendations:** All forms of targeted phototherapy are useful in vitiligo. Good responses were seen in localized involvement, resistant lesions and in children in whom their use is more accepted and convenient (Level of evidence 2+, Grade of recommendation B). Similarly it is useful in psoriasis, either alone or in combination with drugs, even in resistant forms such as palmoplantar psoriasis. In view of expense and practical application, their use is limited to resistant lesions and localized disease. (Level of evidence 2+, Grade of recommendation B). But in other conditions there is no convincing evidence for its use. (Level of evidence 3+, Grade of recommendation C).

Key words: Guidelines, psoriasis, targeted phototherapy, vitiligo

INTRODUCTION

Targeted phototherapy (also called concentrated phototherapy, focused phototherapy and microphototherapy) is a new form of phototherapy which seeks to overcome some of the disadvantages with conventional phototherapy.^[1-4] This modality involves application of light energy directly focused on or targeted at the lesion through special delivery mechanisms such as fiberoptic cables. The term “targeted phototherapy” includes different technologies such as excimer laser (308 nm), intense pulse light systems and non-laser ultraviolet light sources with improved hand-held delivery systems.

Several advantages have been claimed for targeted phototherapy:^[3,5]

- Exposure of involved areas only and sparing of uninvolved areas, thus minimizing acute side effects such as erythema and long-term risk of skin cancer on unaffected skin
- Quick delivery of energy and thereby shortened duration of treatment
- Delivery of higher doses (supererythemogenic doses) of energy because uninvolved areas are not exposed. Higher doses of energy can be delivered selectively to the lesions thereby enhancing efficacy and achieving faster response

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- This has been claimed to shorten duration of treatment leading to less frequent visits to the clinic and thereby lessening inconvenience for the patient
- The maneuverable handpiece allows treatment of difficult areas such as the scalp, nose, genitals, oral mucosa and ear
- Easy administration for children as delivery is hand-held
- Targeted phototherapy machines occupy less space.

However, targeted phototherapy devices have certain disadvantages. They are more expensive. Furthermore, they are not adequate to treat extensive areas given the cost of treatment and time involved. They are not recommended for use if lesions occur over more than 10% of the body area.

Different technologies can deliver targeted phototherapy and these include:

- Excimer laser (xenon chloride laser 308 nm)
- Excimer light (non-coherent monochromatic light source 304–308 nm)
- Non-chromatic ultraviolet light sources (either broadband, 290–310 nm or narrowband, 313 nm).^[5]

The advantages of the light sources over excimer laser include smaller size, lesser maintenance problems and lower cost. Some machines also include the ultraviolet A spectrum and this is an added advantage. Table 1 shows the various indications and contraindications of targeted phototherapy.^[6,7]

METHODS

Relevant literature published until March 2014 was obtained from PubMed, EMBASE and the Cochrane Library. Keywords such as “targeted phototherapy,” “excimer laser,” “excimer lamp,” “non-chromatic ultraviolet light,” “vitiligo” and “psoriasis” were used for literature search. All systematic reviews, meta-analysis, national guidelines, randomized controlled trials, prospective open-label studies and retrospective case series in English were reviewed. The levels of evidence and grades of recommendations for each guideline were according to the format suggested by the British Association of Dermatologists. The studies selected were assessed for their methodology as per the NICE Technical Manual and graded using a

Table 1: Indications and contraindications of targeted lasers

Indications	Contraindications
Localized psoriasis - mainly on chronic plaques	Photosensitive conditions such as lupus erythematosus and xeroderma pigmentosum
Vitiligo - Mainly difficult areas such as ears, under the chin, lips, anal region, oral mucosa, scalp, glans penis and nails	History of cutaneous malignancies
Lichen planus	Patient on arsenic or ionizing radiation therapy
Prurigo nodularis, localized	Patient on photosensitizing drugs
Scleroderma, genital lichen sclerosis	
Alopecia areata	
Atopic dermatitis	
Folliculitis	
Granuloma annulare	
Mycosis fungoides	
Palmoplantar pustulosis	
Pityriasis alba	
CD30+ lymphoproliferative disorder	
Leukoderma	

code “++,” “+” or “-,” based on the extent to which potential biases were minimized. Thereafter, the grade of recommendation was made.

RESULTS

Three hundred and forty studies were evaluated, 24 of which fulfilled the criteria for inclusion in the guidelines.

Therapeutic efficacy in different conditions

Targeted phototherapy has been shown to be effective in several indications [Table 1] wherever conventional phototherapy has been previously used. Some of these indications are discussed below.

Vitiligo

Excimer laser

Low fluencies (50–200 mJ/cm²) were used in vitiligo compared to psoriasis. An initial dose of 200 mJ (150 mJ for women and men under 16 years of age) was used by Shi *et al.*^[8] The subsequent dose was determined as follows: dose increased 20% from treatment 1 to 10, 10% from treatment 11 to 13, 5% from treatment 14 to 16 and 2% from treatment 17 to 20 sessions. If symptomatic erythema or blistering developed, one or two treatments were withheld until resolution of phototoxicity; when treatment was resumed, the dose was reduced to the last well-tolerated dose. Sessions were performed once, twice or 3 times a week. Although administering treatments more frequently (i.e. 2 or 3/week) appears to trigger earlier repigmentation of vitiligo patches, the start of repigmentation appears to depend ultimately on the total number of laser treatment sessions.^[9]

Several studies have demonstrated the efficacy of excimer laser in vitiligo. A pilot study in 2002 showed significant benefits among vitiligo patients in 29 patches of vitiligo from 18 patients. Twenty three vitiligo patches from 12 patients received at least 6 treatments and resulted in some repigmentation in 57% of the treated patches. Eleven vitiligo patches from 6 patients received 12 treatments and resulted in some repigmentation in 82% of the treated patches, with parameters 120 ns, 20 Hz pulse with a 10 mm × 10 mm spot size and a power output of 60 mW of laser light. The study concluded that “the degree of repigmentation in a period of 2–4 weeks is much higher than that achieved with any other present vitiligo therapy”. The xenon chloride excimer laser may represent a new treatment modality for the management of stable vitiligo.^[4] These results were confirmed by other studies which showed benefit with excimer laser in patients of localized vitiligo that had been unsuccessfully treated with other modalities of treatment.^[10] A large study of 140 patients with vitiligo treated by excimer laser showed excellent results in ultraviolet-sensitive areas while ultraviolet-resistant areas such as acral lesions and lesions on joint areas responded poorly.^[11] However, these and other studies were small studies in some patients and uncontrolled.^[12] A meta-analysis comprising seven randomized controlled studies with 390 vitiligo patients showed no significant differences between 308-nm excimer laser and 308-nm excimer lamp when evaluating either $\geq 75\%$ or $\geq 50\%$ repigmentation rate, or between 308-nm excimer laser and narrowband ultraviolet B on either 100% or $\geq 75\%$ repigmentation rate. However, more lesions achieved $\geq 50\%$ repigmentation when treated with 308-nm excimer laser than with narrowband ultraviolet B (level of evidence 1+).^[13]

Excimer light

Several studies have been published which demonstrate the efficacy of excimer light (intense pulsed light). In a pilot study of excimer light in 37 patients of vitiligo, Leone *et al.* obtained initial repigmentation in the first eight treatments and excellent repigmentation in 50% of patients at 6 months.^[14] Some patients who had not previously responded to narrow band ultraviolet B therapy were also found to respond. The results were comparable to excimer laser and superior to narrowband phototherapy. Studies have suggested that combination with topical immunomodulators and fluticasone could enhance the clinical response in vitiligo, especially in more resistant anatomical sites and in segmental vitiligo (level of evidence 1+).^[15-17]

Non-coherent targeted ultraviolet B phototherapy devices

Several non-coherent light sources have been shown to be effective in vitiligo.^[18,19] A study by Akar *et al.* in 32 patients using Daavlin T500x high-dose targeted phototherapy system showed that therapeutic effectiveness is limited and depends on the locations of vitiligo lesions. In this study, only 4 (12.5%) of 32 patients showed visible repigmentation. All the lesions responsive to treatment were facial lesions.^[20] Welsh *et al.* too demonstrated that extremities did not respond satisfactorily.^[21] In a prospective intra-patient placebo-controlled randomized trial, 20% of the lesions treated with narrowband ultraviolet B achieved repigmentation scores above 50% but none of the lesions treated with monochromatic excimer light achieved a repigmentation higher than 50% after 24 sessions (level of evidence 1+).^[22] In a similar multicenter controlled study comparing 308-nm monochromatic excimer light and narrowband ultraviolet B phototherapy, results with 308-nm monochromatic excimer light were superior (level of evidence 1+).^[23]

Summary of recommendations in vitiligo

Evidence suggests that all forms of targeted phototherapy are useful in vitiligo. They can be used in combination with other drugs. However, response is limited to hairy areas and acral, resistant areas are resistant to these new and expensive treatment modalities, too. Hence, these devices may be used in localized areas, in resistant lesions and in children in whom their use is more acceptable and convenient (grade of recommendation B).

Targeted phototherapy in psoriasis

Excimer laser

The initial dose can be calculated by determining the minimal erythema dose for each plaque or fixed doses can be calculated from the thickness of the lesions which are then decreased depending on the clinical improvement. Usually, treatment is started with a dose of light 1–3 times the minimal erythema doses with progressive increase in doses depending on clinical results and tolerance. Selectivity of the laser allows doses to be adapted to each lesion rather than calculated from the minimal erythema dose. The initial dose was maintained until plaques thinned or flattened considerably or pigment appeared. Once plaques thinned or became hyperpigmented (or both), the dose was reduced by 1 minimal erythema dose.^[24-27] Frequency of therapy varied from 1 to 3 sessions per week.

In psoriasis, the efficacy of excimer laser has been confirmed by several reports.^[11,28,29] Localized resistant lesions of psoriasis on elbow and knees were reported to be cleared in as few as 1–3 exposures with moderately long remissions.^[28] Scalp psoriasis was also shown to respond well.^[3] In another study which evaluated patient satisfaction, 55% of patients reported overall satisfaction and 25% reported that laser treatments were better than any other treatment they had tried.^[30] Side effects reported, though usually mild, included burning pain during and after treatment, severe erythema and blistering of the skin.

After a period of initial excitement, subsequent studies have led to a reappraisal of the role of excimer laser in psoriasis.^[31,32] Comparison of excimer laser, excimer lamp and 311-nm narrowband ultraviolet B in patients with psoriasis showed similar clearance and no statistically significant difference in results after 10 weeks of treatment.^[31] The study did show enhanced clearance in the group of patients treated with the excimer laser when they were treated using an accelerated scheme of administration but these patients also had a higher rate of side effects such as blistering and crusting. The study concluded that “the only advantage of laser seems to be the ability to treat exclusively the affected skin and with a reduced cumulative dose, thus perhaps reducing the long term risk of carcinogenicity.” This experience has been confirmed in another similar study.^[33] A study evaluated seven published reports on the use of excimer laser and concluded that there is no consensus for a single excimer laser therapy protocol and as a result, patient preferences should continue to be an important consideration for phototherapy regimen planning (level of evidence 1+).^[34]

Non-laser light sources

Non-laser light sources have proven popular because of their small size and lower costs. Some studies have demonstrated the safety and efficacy of these machines in psoriasis. Both ultraviolet B (narrowband and broadband) and ultraviolet A therapies, alone and in combination with drugs such as calcipotriol and dithranol have been shown to be effective (level of evidence 2+).^[35-42]

Summary of recommendations

All forms of targeted phototherapy are useful in psoriasis, either alone or in combination with drugs, even in resistant forms such as palmoplantar psoriasis.

Given expense and practical application, their use is limited to resistant lesions and localized disease (grade of recommendation B).

Other conditions

Excimer laser has been reported to be effective in other dermatoses also such as oral lichen planus, alopecia areata, atopic dermatitis, mycosis fungoides and lymphomatoid papulosis.^[43-46] Interestingly, excimer laser has been found to be effective in hypopigmented striae, hypopigmented scars, acne vulgaris and other diseases and conditions generally considered difficult to treat.^[47-51] Increase in melanin pigment, hypertrophy of melanocytes and an increase in melanocytes within striae leading to darkening of striae were reported after use of excimer laser.^[52] These results, if confirmed by larger studies, will open up exciting new avenues for the treatment of these important and common cosmetic problems.

Summary of recommendations

Most of these studies are isolated reports in a small number of cases. Hence, the therapy needs to be used after a careful consideration of cost and benefit (grade of recommendation C).

SUMMARY

Targeted phototherapy is an exciting new technology in the management of several dermatological conditions. Their main advantages are safety, ease of administration and suitability for difficult to treat areas and in children. There is no conclusive evidence that they are superior to existing technologies and are also more expensive. Hence, their use may be undertaken in selected cases as outlined.

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Conflicts of interest

There are no conflicts of interest.

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Note from the Chairman, Therapeutic Guidelines Committee

The therapeutic guidelines committee was constituted in 2012 as follows:

Dr. Venkatram Mysore (Chair)

Dr. Rajesh M. Buddhadev

Dr. Satish Pai

Dr. Vinay Saraf

Dr. Krupashankar

Dr. Lalit Kumar Gupta

The following guidelines were prepared:

- a) Leg ulcers, by SIG Leg ulcers (Convener: Dr Reena Rai), published in IJDVL
- b) Urticaria guidelines, by SIG Urticaria (Convener: Dr Kiran Godse), published earlier in IJDVL
- c) Phototherapy: Under publication in IJDVL
- d) Flunasteride use by Dr Venkataram Mysore, Under publication in IJDVL
- e) SJS- TEN, by SIG Drug eruptions (Convener: Dr Lalit Gupta), prepared for publication.

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Dr Venkataram Mysore

President IADVL