Dermatology Online Journal

Volume 16 Number 12
December 2010

DOJ

Contents

Review of home phototherapy

Anand N Rajpara MD[1], Jenna L O'Neill MD[1], Bridgit V Nolan MD[2], Brad A Yentzer MD[1], Steven R Feldman MD PhD[1,3,4]

Dermatology Online Journal 16 (12): 2

1. Department of Dermatology, Wake Forest University School of Medicine, Winston-Salem, North Carolina. arajpara@gmail.com
2. Department of Dermatology, University of Miami
3. Department of Pathology, Wake Forest University School of Medicine, Winston-Salem, North Carolina
4. Department of Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, North Carolina

Abstract

BACKGROUND: Outpatient phototherapy is a safe, effective, and low-cost treatment modality for moderate to severe psoriasis. Barriers to outpatient phototherapy including patient inconvenience, patient co-pays, decreased physician compensation, and insurance disincentive structures have led to decreased use and underutilization of phototherapy. Home phototherapy can potentially overcome many of the barriers associated with outpatient treatment but is not widely used because of concerns over safety and efficacy, lack of resident and physician education, and lack of insurance coverage. PURPOSE: The purpose of this study is to review the use of phototherapy with emphasis on the safety, efficacy, and practical use of home phototherapy. METHODS: A comprehensive Pubmed literature search was done using the keywords NB-UVB, narrowband UVB, BB-UVB, broadband UVB, PUVA, psoralen and UVA, UVA, history of phototherapy, mechanism of phototherapy, phototherapy in dermatology, home phototherapy, and phototherapy for psoriasis. All relevant articles were reviewed. CONCLUSIONS: Home NB-UVB phototherapy can be as safe, effective, and cost-effective as outpatient phototherapy. Further, home UVB is more convenient for patients, has higher patient satisfaction, and a lower treatment burden compared to outpatient phototherapy. Home NB-UVB should be considered as a treatment option for patients eligible for phototherapy.

1. Background

Psoriasis is a chronic inflammatory disease of the skin, scalp, and nails, which affects 1 to 2 percent of the general population. Psoriasis typically first affects patients between the ages of 15 and 35 and can cause major physical and psychological morbidity, leading to a significant economic burden on the health care system and the patient [1, 2, 3, 4]. Psoriasis is a highly variable disease with many forms and various treatment options. Localized disease is generally treated with topical medications whereas generalized disease often requires treatment with phototherapy or systemic agents. Treatment algorithms for psoriasis recommend the use of phototherapy before the use of systemic agents because of the proven safety, efficacy, and low cost of phototherapy.

Unfortunately, many barriers exist to using conventional office based phototherapy, ultimately causing a decline in its use. Phototherapy is sometimes simply inaccessible to patients. Even when patients have access to phototherapy, patient co-pays and inconvenience are major deterrents. Home phototherapy can play a role in treatment by potentially overcoming many of these barriers.

Currently home phototherapy in not widely used because of multiple factors. Physicians and residents may not be well educated about the safety and efficacy of home phototherapy or how to use home phototherapy. Thus, patients may never receive a prescription for home phototherapy. In addition, insurance companies may not cover home phototherapy units and patients' out-of-pocket costs for systemic agents are often lower than those for phototherapy.

The purpose of this article is to review phototherapy as a therapeutic modality, to describe the safety and efficacy of home phototherapy, and to provide physicians with practical information on how to prescribe and monitor home phototherapy treatment.

2. History of phototherapy

The use of sunlight to treat skin disease, also known as heliotherapy, dates back to 1400 B.C. when Hindus in India used plant extracts on the skin followed by sun exposure to treat patients with vitiligo [5, 6]. True phototherapy utilizing an artificial light source did not emerge until the 1890s when Finsen in Denmark used a carbon arc lamp to successfully treat patients with lupus vulgaris [7]. In 1903 Finsen was awarded the Nobel Prize in medicine for his work on lupus vulgaris and he remains the only dermatologist to ever achieve this honor.

In 1925, Goeckerman first described the use of broadband ultraviolet-B (BB-UVB) irradiation combined with topical coal tar in the successful treatment of patients with psoriasis [8]. For almost 50 years the Goeckerman regimen remained the most effective form of phototherapy treatment for psoriasis until the development of PUVA (oral psoralen and UVA irradiation) photochemotherapy. In 1974, Parrish et al reported the successful use of oral psoralen in the form of 8-methoxypsoralen (8-MOP) in combination with UVA irradiation for the treatment of psoriasis [9]. Enthusiasm over the use of UVB phototherapy was rejuvenated in 1988, when narrow-band (NB)-UVB monotherapy was introduced by van Weelden et al and Green at al [10, 11]. Thus, three options have emerged for office-based phototherapy for psoriasis: BB-UVB, NB-UVB, and PUVA.

Home phototherapy for psoriasis was first reported in Sweden in 1979 by Larko and Swanbeck, who successfully used home BB-UVB for the treatment of psoriasis patients that lived too far away to access a clinic [12]. Since then NB-UVB has become the treatment modality of choice for home phototherapy and many open uncontrolled trials evaluating the use of home phototherapy for the treatment of psoriasis have been reported [13, 14, 15]. However, it was not until 2009 that Koek et al reported the first ever single-blinded controlled study comparing office based phototherapy to home phototherapy [16].

3. UV radiation types, psoriasis action spectrum, and systemic phototherapy

Ultraviolet (UV) radiation can be classified into three different types based on wavelength: UVA, UVB, and UVC [17]. UVC has the shortest wavelength (200-290 nm) and is largely absorbed by the ozone. UVB has an intermediate wavelength (290-320 nm) and is the major cause of sunburn. UVA has the longest wavelength (320-400 nm) and can also cause sunburn. Although both UVA and UVB are known carcinogens, PUVA is considered more carcinogenic than UVB radiation [18]. In the UVB range, certain wavelengths between 295 and 313 nm are the most effective at clearing psoriasis. Within that spectrum, the 313 nm wavelength is optimal because it has the smallest ratio of lowest effective daily dose to the minimal erythema dose (MED), defined as the lowest UVB dose that produces perceptible erythema of the entire irradiated skin area [19, 20, 21]. Longer wavelengths added no additional therapeutic benefit and shorter wavelengths detracted from treatment by causing more sunburn [22]. NB-UVB was developed based on these principles and emits wavelengths between 311 nm and 313 nm.

In contrast to NB-UVB, BB-UVB emits wavelengths between 290 nm and 320 nm with a peak at 313 nm [17]. PUVA combines UVA irradiation with orally ingested 8-MOP. UVA irradiation emits wavelengths between 320 nm and 400 nm with a peak at 353 nm. Oral 8-MOP is a systemic photosensitizer that absorbs light optimally between 315 nm and 350 nm [17].

4. Pathogenesis of psoriasis

Psoriasis is a chronic systemic inflammatory disease in which immune dysfunction is thought to play a major role in disease initiation and maintenance [23]. The initial event in psoriasis may involve an unknown antigen, acting in a genetically susceptible host to trigger an inflammatory and immunologic cascade. Stressed keratinocytes release multiple factors that activate dermal dendritic cells, which in turn travel to lymph nodes to activate T-cells via antigen presentation. T-cells then differentiate into Th-1 and Th-17 cells that are attracted by chemokines and adhesion molecules back to the dermis and epidermis. The activated T-cells then activate dendritic cells and macrophages in the dermis and release numerous inflammatory cytokines, including TNF-alpha, IFN-gamma, IL-22, and IL-17, which leads to keratinocyte activation and hyper-proliferation, manifesting clinically as psoriatic plaques [23].

5. Mechanism of UV radiation in treating psoriasis

UVB and UVA both penetrate into the epidermis and papillary dermis and have various effects on keratinocytes, T-cells, and Langerhans cells. The longer wavelength of UVA allows it to penetrate into the deep dermis affecting dermal dendritic cells, dermal fibroblasts, endothelial cells, mast cells, and granulocytes [24]. The mechanisms of UVB and PUVA in treating psoriasis are similar and can be categorized into immediate cytopathic effects and delayed immunosuppressive effects [25].

The immediate effects of UV radiation are largely cytopathic and include induction of cell-cycle arrest in hyperproliferative epidermal cells and T-cell apoptosis. UVB directly damages DNA and produces thymidine dimers that interfere with DNA replication, transcription, and translation [25]. Similarly, psoralen intercalates between DNA base-

pairs and forms psoralen DNA cross-links upon UVA exposure [26, 27]. UV radiation also generates reactive oxygen species, which damage cell machinery and cell membranes via lipid peroxidation [28, 29, 30]. As a result, UV radiation reduces DNA, RNA, and protein synthesis leading to decreased mitosis in epidermal cells [31, 32]. Further, UVB and PUVA both can cause apoptosis of T-lymphocytes that play an integral role in the pathogenesis of psoriasis [33, 34].

UV radiation also treats psoriasis through delayed immunosuppressive effects. UV radiation decreases the number of activated Langerhans cells by 90 percent after 7 treatment sessions [35]. Remaining dendritic cells are unable to effectively activate T-cells [25]. UVB also down-regulates Th-17 cells [36]. Further, UV radiation alters the cytokine secretion pattern of macrophages leading to up-regulation of IL-10, which aids in switching the predominant Th-1 response in psoriasis to a Th-2 type response [37]. UVB also suppresses the expression of adhesion molecules on antigen presenting cells in the skin [38, 39]. Thus, UV radiation treats psoriasis by decreasing the number and activity of both T-cells and dendritic cells, increasing secretion of anti-inflammatory cytokines, decreasing inflammatory cell trafficking by downregulating adhesion molecules, and by switching the Th-1 immune response to a Th-2 response.

6. When to consider systemic phototherapy

Traditionally, psoriasis is classified into mild, moderate, and severe disease based on the percentage of body surface area (BSA) involved: mild <2 percent, moderate 2-10 percent, or severe >10 percent [40]. Other factors such as the patient's quality of life and the location of lesions should also be taken into account when evaluating a patient's disease severity [40]. Topical medications are used as first-line agents to treat localized, mild disease. Moderate to severe disease or mild disease not responsive to topical treatments generally warrants some form of systemic treatment in addition to topical therapy [41]. Options for systemic treatment of psoriasis include phototherapy, conventional systemic therapy (i.e., methotrexate, cyclosporine, acitretin), and newer biologic therapies (i.e., alefacept, efalizumab, entanercept, ustekinumab). Established treatment algorithms recommend that patients with moderate to severe plaque or guttate psoriasis requiring systemic therapy first receive a trial of phototherapy [42]. Conventional systemic agents like methotrexate are also effective and inexpensive, but have potentially serious side-effects. Biologic therapies are efficacious and safe in the short-term, but they are very costly and newer agents have unknown long-term safety profiles in the treatment of psoriasis. The efficacy, safety, and cost of office-based phototherapy will be discussed in the following sections.

7. Efficacy of office based phototherapy: BB-UVB, NB-UVB, and PUVA

Adrian et al reported that 18 out of 20 subjects with psoriasis achieved complete clearance with BB-UVB three times a week in combination with white petrolatum. [43]. Similarly, 26 out of 26 subjects with plaque-type psoriasis were cleared of disease using UVB five times a week with white petrolatum, in an average of 27 treatments [44]. BB-UVB administered three to five times weekly produces clearance in an average of 20-25 treatments, with initial improvement

usually noted within 4 weeks of initiating therapy [45]. The remission rate of psoriasis 1 year after BB-UVB phototherapy is estimated to be about 5 percent [45].

The efficacy of NB-UVB monotherapy was primarily evaluated by trials that used split body comparisons of NB-UVB with BB-UVB. Coven et al performed split body comparisons of NB-UVB versus BB-UVB, both with and without coal tar in 22 subjects with psoriasis [46]. Clinical clearance of psoriasis occurred in 86 percent of NB-UVB treated sites versus 73 percent of BB-UVB treated sites [46]. Histopathological resolution occurred in 88 percent of lesions treated with NB-UVB versus 59 percent treated with BB-UVB [46]. Clinical resolution of psoriasis was more rapid in the NB-UVB treated sites [46]. In another study of 11 subjects, clinical clearance occurred in 81.8 percent of NB-UVB treated sites versus 9.1 percent of BB-UVB treated sites [47]. Further, 75 percent of subjects showed reversal of epidermal hyperplasia on NB-UVB treated sites compared with none on the BB-UVB treated sites [47]. Green et al and Larko found no differences in the efficacy of NB-UVB versus BB-UVB but both reported that lesions treated with NB-UVB cleared faster and subjects either preferred NB-UVB or had no preference [11, 48]. NB-UVB administered three to five times weekly produces clearance in an average of 15-20 treatments, with initial improvement usually seen after eight to ten treatments [45]. The remission rate of psoriasis 1 year after NB-UVB phototherapy is estimated to be about 38 percent but may increase with maintenance therapy [12, 45].

The efficacy of PUVA was demonstrated by two large multicenter studies. In a European study of 3175 subjects with severe psoriasis treated with PUVA, 88.8 percent of subjects achieved better than marked clinical improvement [49]. On average, twenty exposures over 5.3 weeks with a total cumulative UVA dose of 96 J/cm² were required for clearing [49]. In a U.S. study of 1308 subjects with psoriasis treated with PUVA, 88 percent of subjects achieved clearance [50]. Depending on whether the subject received PUVA therapy 2 times a week or 3 times a week, on average 18 to 20 treatments over 8-10 weeks with a total cumulative UVA dose of 173 to 201 J/cm² was required for clearing [50]. Although both studies demonstrated the efficacy of PUVA therapy, in the U.S. PUVA study investigators needed higher cumulative UVA doses and longer treatment times to achieve disease clearance. These differences can be attributed to the fact that the U.S. study used Fitzpatrick skin type to determine initial dosing and used fixed dosage increases, where as the European study used the MED to determine initial dosage and used individualized dosage increases based on skin reactions [49, 50]. Two systematic reviews of the large majority of PUVA studies confirmed the efficacy of PUVA to be between 70 percent and 100 percent [51, 52]. PUVA treatment two to three times per week produces clinical clearance in an average of 5-12 weeks, with initial improvement typically seen in 1 month [45]. PUVA typically induces remission of disease for 3 to 12 months [45].

8. Safety of office-based phototherapy

The short-term side effects of UVB and UVA irradiation are similar. They include erythema, swelling, dry skin, pruritus, and rarely phototoxic blisters and increased recurrence of herpes simplex virus [45, 53]. UVB-induced erythema peaks before 24 hours, whereas PUVA-induced erythema peaks at 48-96 hours. Exposure of the eye to UVB can cause photokeratitis; exposure to UVA may cause cataracts, especially in children. Patients must wear UV protective goggles while

undergoing phototherapy. Patients undergoing oral PUVA therapy should be instructed to protect their eyes from UV light for up to 24 hours after ingesting oral psoralen because the photosensitizer [45, 53].

UVB may be associated with an increased risk of genital tumors in both sexes, whereas UVA elevates the risk of male genital squamous cell cancer [18, 54]. All patients must wear genital shields when receiving phototherapy. In addition to the aforementioned acute side-effects, short-term side effects associated with oral psoralen include nausea and vomiting, and rarely, elevated liver enzymes, drug fever, exanthema, headaches, dizziness, and bronchoconstriction [53].

Long-term side effects of phototherapy include photoaging and carcinogenesis. UVB and PUVA may lead to wrinkle formation, telangectasias, lentigines, elastosis, xerosis, and pigmentary changes [45, 53]. PUVA may also cause excessive hair growth [49, 55]. A major concern is the risk of cutaneous malignancy associated with UV exposure. Currently, there is no evidence indicating that UVB phototherapy is associated with an increased risk of melanoma or non-melanoma skin cancer (NMSC) [56, 57]. A recent study examined 3867 subjects with a median number of 29 NB-UVB treatments and found that there was no association between NB-UVB and squamous cell cancer (SCC), basal cell cancer (BCC), or melanoma with a median follow-up of 5.5 years [58]. However, longer follow-up times may be needed to detect an increased rate of carcinogenesis after phototherapy.

On the contrary, there is strong evidence that high cumulative PUVA exposure is associated with a dose-related increase in the risk of non-melanoma skin cancer, particularly SCC [59, 60, 61]. In a Swedish follow-up study of 4799 subjects who had received PUVA between 1974 and 1985, the relative risk of SCC was 5.6 for men and 3.6 for women followed for an average of 15.9 years and 16.2 years, respectively [62]. A meta-analysis of PUVA therapy in non-Caucasians revealed no increased risk of NMSC in this population [63].

Absolute contraindications to the use of UVB phototherapy are known lupus erythematosus and xeroderma pigmentosum [45]. Relative contraindications to UVB use include a history of melanoma, young age, cardiovascular disease, severe infirmity, bullous disease, and photosensitizing medications [53]. UVB is considered safe in pregnant and lactating women [45]. Monitoring during treatment includes routine full skin examinations [45].

Absolute contraindications to the use of PUVA therapy are known lupus erythematosus, xeroderma pigmentosum, family or personal history of melanoma, pregnancy, and lactation. Oral psoralen has a pregnancy category C rating. Relative contraindications to PUVA use include young age, cardiovascular disease, severe infirmity, bullous disease, kidney disease, liver disease, and photosensitizing medications. Baseline and periodic monitoring includes full skin examination and yearly eye examination; eye examination may be more frequent if the patient is non-compliant with UV eye protection or experiences new vision problems [45].

9. Cost of office-based phototherapy

In the pre-biologic era, the cost of psoriasis to the health care industry was estimated to be almost 3 billion dollars with an estimated cost of 800 dollars per patient per year [64]. With the advent of

biologic therapies these estimates are likely much larger. Feldman et al provided a financial comparison of different treatment options for psoriasis in the U.S. They concluded that methotrexate was the least expensive treatment for psoriasis at an estimated cost of $1,600 per year per patient, whereas NB-UVB and PUVA were the second least expensive treatment options costing $3,700 and $4,700, respectively [65]. In comparison, the biologic therapies were estimated to cost more than 20,000 dollars per year per patient [66]. There are several effective treatment modalities for moderate to severe psoriasis that have achieved at least a 75 percent reduction in the psoriasis area and severity index (PASI) in 70 percent of subjects in clinical trials. In a cost comparison of all of these treatment modalities for moderate to severe psoriasis, phototherapy was the second cheapest treatment option for moderate to severe psoriasis behind methotrexate [65]. Further, all other effective treatments for moderate to severe psoriasis cost at least a third more than phototherapy, with the exception of methotrexate [65].

10. Dosage and scheduling for office based phototherapy

Dosing and scheduling of office based phototherapy can be determined by using either Fitzpatrick skin type or MED. In general, MED based phototherapy protocols are thought to be safer than skin type based protocols but most physicians prefer the latter because it is more convenient [25]. BB-UVB protocols based on skin type have initial doses of 20-60 mJ/cm² with subsequent increases of 5-30 mJ/cm² after each treatment session [45, 67]. BB-UVB protocols based on MED have an initial dose of 50 percent MED with subsequent increases by 25 percent of the initial MED after each treatment for the first 10 treatments then increases by 10 percent for the next 10 treatments [45, 67]. A single course of BB-UVB phototherapy consists of 3 to 5 sessions per week for a typical duration of 20 to 25 treatments [45].

NB-UVB protocols based on skin type have initial doses of 130-400 mJ/cm² with subsequent increases of 15-65 mJ/cm² after each treatment session [45, 67]. NB-UVB protocols based on MED have an initial UVB dose of 50 percent MED with subsequent increases by 10 percent of the initial MED after each treatment session [45, 67]. A single course of NB-UVB phototherapy consists of 3 to 5 sessions per week for a total duration of 15 to 20 treatments [45].

For PUVA photochemotherapy, oral 8-MOP dosing is weight-based; 0.4-0.6 mg/kg is taken one to two hours before UVA exposure [45]. Using skin type based protocols, the initial UVA dose is 0.5-3.0 J/cm² with subsequent increases of 0.5-1.5 J/cm² after each treatment session [45, 67]. Oral PUVA protocols based on MED have initial UVA doses of 0.5-0.7 MED with individualized dosage increases not exceeding 30 percent MED twice a week [25]. A single course of oral PUVA treatment consists of 2 to 3 sessions per week for a total of 20 to 25 treatments [45].

11. Comparing phototherapy treatment options: BB-UVB vs. NB-UVB vs. PUVA

In the split body trials discussed earlier NB-UVB had several advantages over BB-UVB including higher efficacy, faster clearance, and greater patient preference [11, 12, 46, 47, 48]. Thus, NB-UVB is preferred over BB-UVB for the treatment of psoriasis [45].

The comparison of NB-UVB phototherapy and PUVA photochemotherapy is more complicated. An early study using split body comparisons of PUVA and NB-UVB in 10 subjects found the two therapies to be equally effective, but subjects preferred NB-UVB treatment [68]. These results were confirmed in 25 subjects with chronic plaque-type psoriasis and mean PASI score of 16, however a subset of subjects with high baseline PASI scores responded significantly better to PUVA [69]. An open-label trial of 52 subjects comparing twice-weekly NB-UVB with PUVA showed equal efficacy, whereas a larger trial of 100 subjects found PUVA to be more effective than NB-UVB in clearing disease [70, 71]. In a randomized, double-blind, controlled study of 93 subjects comparing NB-UVB to PUVA both used twice weekly, PUVA was significantly more effective than NB-UVB at achieving disease clearance (84% versus 65%) and did so with fewer treatments (17.0 versus 28.5). Further, disease remission rate six months after stopping therapy was significantly higher in the PUVA group (68% versus 35%) [72]. PUVA may induce disease remission for four to six to months after stopping treatment [22, 50, 73]. More frequent NB-UVB administration in clinical practice may affect efficacy and remission results.

PUVA may be more efficacious than NB-UVB in treating psoriasis, particularly in subjects with severe disease located on the extremities [68, 69, 71, 72]. This may be attributed to the fact that UVA radiation penetrates more deeply into thick plaques than NB-UVB. Further, longer disease remission is achieved with PUVA compared to NB-UVB [22, 50, 72, 73]. Still, NB-UVB has many advantages over PUVA. NB-UVB is more convenient and is preferred by patients [68]. Unlike PUVA, no oral medication is required with NB-UVB. Short- and long-term side effects are also less frequent with NB-UVB compared to PUVA [45]. NB-UVB can be used safely in pregnant and lactating women, unlike PUVA, which is contraindicated in such circumstances [45]. As a result, accepted treatment algorithms for psoriasis recommend a trial of NB-UVB phototherapy before PUVA photochemotherapy [42]. NB-UVB phototherapy is also the preferred modality for home phototherapy because of its greater safety and convenience. However, for severe, resistant disease that fails to respond to NB-UVB, PUVA should be considered as a next step in treatment [42].

12. Barriers to outpatient phototherapy treatment

Despite the efficacy, safety, and low cost of phototherapy, this treatment modality may be underutilized for psoriasis. Data from the National Ambulatory Medical Care Survey indicate that physician visits for phototherapy decreased from 873,000 in 1993-1994 to 53,000 in 1997-1998 [74]. In a 2006 survey of 1.5 million National Psoriasis Foundation members, only one third of patients reported ever undergoing phototherapy [75]. The decreasing use and underutilization of phototherapy for moderate to severe plaque psoriasis may be caused by multiple factors related to the patient, the physician, and the insurance company [76].

From a patient's perspective, outpatient phototherapy is highly inconvenient. Phototherapy is time consuming and may cause patients to miss time from work or family. In addition to the inconvenience, patients are required to shell out co-pays at each treatment session. Co-pays discourage patients from choosing phototherapy and lead to decreased use of this treatment modality [15, 77]. From the doctor's perspective, phototherapy may not be economically viable. Declining reimbursement

rates in combination with the higher cost of new, more efficacious NB-UVB office units, the need for trained phototherapy staff, and the hassle of obtaining patient coverage may deter physicians from prescribing phototherapy [74, 76]. Further, insurance company incentive structures discourage prescribing phototherapy despite the higher cost of biologic agents [74, 76]. Estimates of the first year out-of-pocket cost per patient per year are $3,040 for office phototherapy and $920 for biologic therapy, whereas the cost to the insurance company is $76 for outpatient phototherapy and $23,408 for biologic therapy [78]. Consequently, the barriers to outpatient phototherapy may be pushing patients and physicians away from this safe, effective, and low cost treatment modality [74, 76].

13. Home NB-UVB phototherapy: opinions and misinformation

Home NB-UVB phototherapy has the potential to overcome many of the barriers associated with traditional outpatient phototherapy but its use remains controversial. In 2006, Koek et al found opinions of dermatologists regarding home phototherapy to be largely negative, despite a lack of controlled trials evaluating home phototherapy [79]. All five national guidelines regarding the use of home phototherapy are worded cautiously and recommend restricting its use to certain select patients [79, 80, 81, 82, 83]. In the various guidelines, reasons for restricting the use of home phototherapy include lack of medical supervision, lower efficacy, higher attendant risk, and medico-legal liability [79]. Of 367 dermatologists surveyed, 55 percent regarded home UVB to be inferior to outpatient UVB and 33 percent felt that home UVB carried more risk than outpatient UVB phototherapy [16,79]. At the time of the study by Koek et al there were no controlled trials comparing home to outpatient phototherapy and thus the negativity regarding home phototherapy was based largely on opinion rather than evidence.

14. PLUTO Study

In 2009 the first multicentre, single-blind, randomized, controlled non-inferiority trial was performed comparing home to outpatient NB-UVB phototherapy for the treatment of mild to severe psoriasis [16]. One hundred and ninety six patients with plaque or guttate psoriasis were selected based on eligibility for NB-UVB phototherapy as determined by their prescribing dermatologist. Subjects were then randomized to either outpatient phototherapy at a local hospital or home phototherapy. Dosing and scheduling of NB-UVB for the outpatient group was left to the discretion of the hospital, whereas dosing and scheduling of the home phototherapy group was left to the discretion of the home care institution that provided the home NB-UVB units. Upon delivery of the home NB-UVB unit, each patient underwent a 30-60 minute nurse education session on proper use of the device, and a treatment schedule was provided with time in seconds for each irradiation. Subsequent treatments were altered by the home care nurse based on patient response. For both groups, treatment was considered finished after a single course of NB-UVB had been administered. The main outcome measure of the study was efficacy as determined by a 50 percent reduction in PASI and self-administered PASI (SAPASI) from baseline. Other outcomes measured were dosimetry, short-term side effects, quality of life, treatment burden, and patient preference and satisfaction.

15. Efficacy of home phototherapy

Early studies on home phototherapy found it to be effective in treating psoriasis. In 1969 Larko and Swanbeck treated 28 subjects with severe psoriasis using home BB-UVB, which successfully cleared disease in 20 of the subjects [12]. In 1981 Jordan et al treated 56 subjects with severe psoriasis using home BB-UVB and coal tar and achieved disease clearance in 55 of the subjects [13]. In 2002 Cameron et al treated 23 subjects with plaque psoriasis using home NB-UVB and achieved disease clearance in 18 of the subjects [15].

The PLUTO study found home and outpatient NB-UVB phototherapy to be equally effective. PASI 50 and SAPASI 50 were reached by 70 percent and 82 percent of the home treatment group, respectively, compared to 73 percent and 79 percent of the outpatient group. PASI 75 and SAPASI 75 were reached by 41 percent and 69 percent of the home treatment group, respectively, compared to 42 percent and 59 percent of the outpatient group. PASI 90 and SAPASI 90 were reached by 20 percent and 44 percent of the home treatment group, respectively, compared to 19 percent and 30 percent of the outpatient group [16]. The mean duration of therapy for home phototherapy was 11 weeks as compared to 14 weeks for outpatient phototherapy [16].

16. Safety of home phototherapy

In the PLUTO study, short term safety was assessed by measuring the incidence of acute side effects via patient diaries, including erythema, blistering, and burning sensation. There was no difference in the incidence of acute side effects between the home and outpatient groups, with 87 percent of all subjects reporting mild erythema, 56 percent burning sensations, 36 percent severe erythema, and 6 percent blistering [16]. Long-term safety was assessed by measuring the total cumulative UVB light dose that each patient received. The mean cumulative dose of UVB per subject at the end of treatment was 51.5 J/cm² in the home group as compared to 46.1 J/cm² in the outpatient group, which was not statistically significant [16]. When surveyed regarding the safety of home UVB treatment, 32 percent of the home phototherapy subjects felt home UVB therapy was very safe, 52 percent felt it was safe, 16 percent were impartial, and no subjects felt it was unsafe [16].

The authors point out that the study did not address the concern of continued, unsupervised use of home NB-UVB after the end of treatment because home care institutions delivered and retrieved phototherapy units at the beginning and end of therapy [16]. There are other ways of addressing this issue. In a trial of home NB-UVB combined with oral acitretin for the treatment of moderate to severe psoriasis, Yelverton et al used home units that electronically provided subjects with only a set number of treatments [84]. Once the treatments had finished, the subjects had to contact their physician for a code to obtain additional treatments. This safety feature is known as a controlled prescription timer (CPT). Other safety features on home NB-UVB units include key locked ON/OFF switches to prevent unauthorized use, timers that limit treatments to a maximum of 10 or 20 minutes, dosimeter controls for accurate dosing, acrylic safety shields to prevent contact with UV bulbs, and failsafe switches that disable the unit in the event of an emergency [85].

Earlier studies of home phototherapy also endorse its safety. Jordan et al reported no significant phototoxic episodes in 56 subjects treated with home UVB [13]. In another study of 30 subjects (23 with psoriasis) receiving home phototherapy, 62 percent experienced grade 1 erythema, 42 percent grade 2 erythema, 26 percent grade 3 erythema, and none experienced grade 4 erythema [15]. Self-reported side effects in 25 subjects receiving home NB-UVB included erythema (36%), pruritus (8%), blisters or dryness (1%); 56 percent reported no side effects [86].

17. Cost of home phototherapy

In a cost analysis of the PLUTO study, home NB-UVB was not more costly than outpatient NB-UVB. The average total cost per subject was €752 ($920) for outpatients and €800 ($980) for subjects treated at home [87]. However, the cost analysis did not account for costs associated with time missed from work. In a scenario cost analysis that included the cost of work absence, the cost of home phototherapy was €838 ($1,025) per subject whereas outpatient phototherapy was €1362 ($1,667) per subject [87]. Further, the total cost of home phototherapy included the cost of services provided by the home care institution services, including delivery and pick-up of the home NB-UVB unit. In a payer prospective cost model it was estimated that within two years of treatment initiation, home NB-UVB phototherapy was the least expensive treatment modality for severe psoriasis [88].

18. Advantages of home NB-UVB: patient satisfaction and lower treatment burden

In the PLUTO study patient satisfaction and preference were greater with home NB-UVB compared to outpatient phototherapy. Of subjects treated at home, 43 percent rated their experience as excellent compared to 23 percent of the outpatient group [16]. Ninety two percent of subjects receiving home phototherapy and 60 percent of subjects treated in an outpatient setting stated they would prefer home NB-UVB in the future [16]. In another survey of 25 subjects receiving home NB-UVB for a variety of photo-responsive diseases, 96 percent of subjects found home phototherapy to be effective and all subjects stated they would continue home phototherapy, would repeat treatment if necessary, and would recommend home phototherapy to other patients [86].

Quality of life as measured by the psoriasis disability index and the SF-36 (a generic general health survey with eight domains) was equally improved over the study duration in both the home and outpatient treatment groups [16]. Burden of treatment was also assessed via a survey that allowed subjects to rate four aspects of treatment (treatment method, UVB phototherapy, time lost, and entire treatment) on a 0 to 10 scale. The treatment burden associated with home phototherapy was significantly less than outpatient phototherapy in all four aspects of treatment by an average of 1.23 to 3.01 points [16]

19. Home phototherapy: Convenience and adherence

Home phototherapy is convenient for a number of reasons:

treatment can be performed in the patient's home at a convenient time, time away from work and family is minimized, and costs associated with clinic visits and travel are avoided. In a survey of 25 subjects receiving home NB-UVB, the main reasons for choosing home phototherapy over outpatient phototherapy were time, travel expenses, and difficulty with work schedule [86]. Subjects undergoing outpatient phototherapy described the treatment as inconvenient and 75 percent of those surveyed reported home phototherapy would be helpful [15]. Patients generally prefer treatment modalities that are less time consuming, do not involve having to miss work, and have less out-of-pocket expense [66].

Adherence to home versus outpatient phototherapy has not been studied. However, one would expect that patients would be equally or more adherent with home phototherapy because of its greater convenience and patient satisfaction. Adherence to home phototherapy can now be measured using an electronic data logger with a photo-sensor that accurately records the usage of home phototherapy units [89]. In fact, a recent study demonstrated adherence to home NB-UVB phototherapy to be higher than adherence to oral acitretin [90]. Twenty-seven subjects with moderate to severe psoriasis were treated with 10 to 25 mg of oral acitretin daily and home NB-UVB three times a week for twelve weeks. Adherence to acitretin was measured using electronic monitoring medication bottle caps and adherence to phototherapy was assessed using the electronic data logger. Mean adherence to acitretin decreased steadily over the twelve week treatment period whereas adherence to NB-UVB phototherapy remained steady [90].

20. Before starting home phototherapy

Any patient eligible for outpatient NB-UVB phototherapy is also a candidate for home phototherapy. Patients being considered for home phototherapy should undergo a trial of office-based NB-UVB first to assess whether the patient's disease responds to treatment. When purchasing a home NB-UVB phototherapy unit, there are several different types of NB-UVB home units and suppliers to choose from. Different home units have varying convenience features, safety features, efficacy, and prices. Depending on the location of psoriatic involvement, whole body units, scalp units, or hand and foot units are available. A review of various home phototherapy units is provided in Table 1, and a list of suppliers can be found at the National Psoriasis Foundation website [91-97].

Before initiating home phototherapy, patients require a full body skin examination and basic phototherapy education as would occur prior to outpatient phototherapy. The importance of wearing UV protective goggles, genital shields if male, and nipple shields if female should be emphasized. In addition, patients should be trained to recognize adverse events such as severe erythema or blistering. Patients should be instructed to contact the dermatologist in the event of a side effect so that treatment may be initiated and UVB dosing may be altered. Patients also must be made aware of the importance of maintaining a proper distance of 12 inches from the UV bulbs so that they receive an accurate UVB dose. Finally, the patient must agree to have regular follow-up visits so that the dermatologist can monitor response to therapy and side effects, alter UVB dosing if necessary, and conduct routine skin checks for skin cancer [85].

21. Home phototherapy protocols: Scheduling and dosing

A standard schedule for home NB-UVB phototherapy for psoriasis consists of three sessions per week; treatment frequency of every other day is most effective based on experience [85]. UVB dosing and treatment times for home phototherapy can be calculated according to the MED or Fitzpatrick skin type. Most physicians prefer using a Fitzpatrick skin type-based phototherapy regimen because it is more convenient [25]. In a Fitzpatrick skin type based regimen, initial treatment time and dose are based on the patient's skin type [85, 98]. Fitzpatrick skin types are described in Table 2. Initial NB-UVB treatment times based on skin type are presented in Table 3. Subsequent alterations in UVB treatment times are based on patient response to treatment and patient skin type. If the patient experiences no erythema, the treatment time can be increased according to skin type. Increases in NB-UVB treatment time based on skin type are presented in Table 4. The presence of slight erythema warrants no change in treatment time. Finally, if the patient experiences severe erythema or sunburn, phototherapy should be discontinued until the erythema resolves. Therapy can then be resumed using a treatment time that is one half of the most recent treatment time [85].

Home NB-UVB phototherapy based on MED is safer than skin type-based regimes but is less convenient [25]. The initial treatment dose is most frequently 0.7 MED but may range from 0.5 - 1.0 MED [99-104]. Subsequent increases in UVB dosage and treatment time depend on the dermatologist and patient and can vary from increases of 10 to 20 percent in the UVB dosage with each treatment session [85, 105]. With both MED-based and skin type-based home phototherapy, treatment should continue until there is complete disease clearance or no further improvement can be attained [85, 101].

22. Medico-legal issues

Medico-legal issues should not be an impediment to prescribing home phototherapy. Home phototherapy is equally safe and as effective as outpatient phototherapy, both of which are potentially much safer than other treatment options for moderate to severe psoriasis. As with any psoriasis treatment, proper patient selection should be considered to assure compliance with both the home phototherapy treatment regimen and with regular follow up visits. With appropriate patient selection and regular clinical follow-up, home phototherapy is a safe and effective treatment modality with low risk of medical or legal liability.

23. Barriers to home phototherapy

The use of home NB-UVB phototherapy for psoriasis is not widespread and as of 2002 physicians were prescribing an estimated 10 times more biologic therapy than home phototherapy [74]. Further barriers to the use of this treatment modality include inadequate physician and resident education and lack of insurance coverage. A survey at the 9th Annual Dermatology Chief Residents' Meeting revealed that only 35 percent of dermatology residents received formal training regarding the use and prescribing of home phototherapy [85]. Further, 73 percent of dermatology residents had never prescribed a home phototherapy unit during their training [85]. In a survey of 167 physicians who wrote more than 80 prescriptions for entanercept in

2006, 20 percent replied that they were unaware of home phototherapy or how to prescribe it [85]. Resident and physician education regarding home phototherapy needs to be improved.

Without insurance coverage, a UVB home phototherapy unit carries an out-of-pocket expense of $2,000 or more for the patient [85]. With partial insurance coverage under durable medical equipment, a term used to define any form of medical equipment that can be used at home to improve quality of life, a patient may still have to pay $1,000 [85]. Although this is a one time expense, many patients cannot afford it. In an analysis of thousands of home phototherapy prescriptions, 43 percent of patients never ended up purchasing a home unit, of whom 73 percent cited high out-of-pocket expense as the reason for not filling their prescription [85]. In addition, of the 167 physicians who wrote more than 80 prescriptions for entanercept in 2006, 62 percent stated they prescribed less home phototherapy because of the high out-of-pocket expenses for the patient [85].

Insurance company incentive structures actually make it less expensive for patients to utilize biologic therapies rather than home phototherapy for moderate to severe psoriasis [74, 76]. It was estimated that the first year out-of-pocket cost per patient was $2,590 for home phototherapy and $920 for biologic therapy, whereas the cost to the insurance company was $5 and $23,408, respectively [78]. Of the 43 percent of patients who did not end up using their prescription for a home phototherapy unit, 44 percent stated they would use biologics instead because of a lower copay [85].

24. Conclusion

Outpatient phototherapy for moderate to severe psoriasis is safe, effective, and cost-effective but its use is significantly decreasing because of patient inconvenience, patient co-pays, decreasing physician compensation, and nonsensical insurance incentive structures. As a result, established treatment algorithms are being disregarded and patients are being started directly on biologic agents. Home NB-UVB phototherapy has emerged as a safe, effective, and low cost treatment method that overcomes many of the barriers associated with traditional outpatient phototherapy. Home NB-UVB has the potential to re-establish phototherapy in the psoriasis treatment algorithm and offers patients a treatment method that is both convenient and potentially safer than biologic therapy. Widespread use of home NB-UVB for moderate to severe psoriasis is not only in the best interest of patient care, but will also potentially lower healthcare costs drastically for years to come.

References

1. de KJ, Sprangers MA, Mombers FM, et al. Quality of life in patients with psoriasis: a systematic literature review. J Investig Dermatol Symp Proc 2004 Mar;9(2):140-7. [PubMed]

2. Griffiths CE, Richards HL. Psychological influences in psoriasis. Clin Exp Dermatol 2001 Jun;26(4):338-42. [PubMed]

3. Rapp SR, Feldman SR, Exum ML, et al. Psoriasis causes as much disability as other major medical diseases. J Am Acad Dermatol 1999 Sep;41(3 Pt 1):401-7. [PubMed]

4. Javitz HS, Ward MM, Farber E, et al. The direct cost of care for

psoriasis and psoriatic arthritis in the United States. J Am Acad Dermatol 2002 Jun;46(6):850-60. [PubMed]

5. Roelandts R. The history of phototherapy: something new under the sun? J Am Acad Dermatol 2002 Jun;46(6):926-30. [PubMed]

6. Fitzpatrick TB, Pathak MA. Historical aspects of methoxsalen and other furocoumarins. J Invest Dermatol 1959 Feb;32(2, Part 2):229-31. [PubMed]

7. Saleeby CW. Sunlight and health. New York, London, G.P. Putnam's Sons, 1924.]

8. Perry HO, Soderstrom CW, Schulze RW. The Goeckerman treatment of psoriasis. Arch Dermatol 1968 Aug;98(2):178-82. [PubMed]

9. Parrish JA, Fitzpatrick TB, Tanenbaum L, et al. Photochemotherapy of psoriasis with oral methoxsalen and longwave ultraviolet light. N Engl J Med 1974 Dec 5;291(23):1207-11. [PubMed]

10. van WH, De La Faille HB, Young E, et al. A new development in UVB phototherapy of psoriasis. Br J Dermatol 1988 Jul;119(1):11-9. [PubMed]

11. Green C, Ferguson J, Lakshmipathi T, et al. 311 nm UVB phototherapy--an effective treatment for psoriasis. Br J Dermatol 1988 Dec;119(6):691-6. [PubMed]

12. Larko O, Swanbeck G. Home solarium treatment of psoriasis. Br J Dermatol 1979 Jul;101(1):13-6. [PubMed]

13. Jordan WP, Jr., Clarke AM, Hale RK. Long-term modified Goeckerman regimen for psoriasis using an ultraviolet B light source in the home. J Am Acad Dermatol 1981 May;4(5):584-91. [PubMed]

14. van Vloten WA. [Home treatment of psoriasis using ultraviolet-B irradiation]. Ned Tijdschr Geneeskd 1993 Dec 4;137(49):2525-6. [PubMed]

15. Cameron H, Yule S, Moseley H, et al. Taking treatment to the patient: development of a home TL-01 ultraviolet B phototherapy service. Br J Dermatol 2002 Nov;147(5):957-65. [PubMed]

16. Koek MB, Buskens E, van WH, et al. Home versus outpatient ultraviolet B phototherapy for mild to severe psoriasis: pragmatic multicentre randomised controlled non-inferiority trial (PLUTO study). BMJ 2009;338:b1542. [PubMed]

17. Sage RJ, Lim HW. UV-based therapy and vitamin D. Dermatol Ther 2010 Jan;23(1):72-81. [PubMed]

18. Studniberg HM, Weller P. PUVA, UVB, psoriasis, and nonmelanoma skin cancer. J Am Acad Dermatol 1993 Dec;29(6):1013-22. [PubMed]

19. Bandow GD, Koo JY. Narrow-band ultraviolet B radiation: a review of the current literature. Int J Dermatol 2004 Aug;43(8):555-61.

[PubMed]

20. Parrish JA, Jaenicke KF. Action spectrum for phototherapy of psoriasis. J Invest Dermatol 1981 May;76(5):359-62. [PubMed]

21. Diffey BL, Farr PM. An appraisal of ultraviolet lamps used for the phototherapy of psoriasis. Br J Dermatol 1987 Jul;117(1):49-56. [PubMed]

22. van WH, Young E, van der Leun JC. Therapy of psoriasis: comparison of photochemotherapy and several variants of phototherapy. Br J Dermatol 1980 Jul;103(1):1-9. [PubMed]

23. Nestle FO, Kaplan DH, Barker J. Psoriasis. N Engl J Med 2009 Jul 30;361(5):496-509. [PubMed]

24. Krutmann J. Therapeutic photoimmunology: photoimmunological mechanisms in photo(chemo)therapy. J Photochem Photobiol B 1998 Jul 10;44(2):159-64. [PubMed]

25. Schneider LA, Hinrichs R, Scharffetter-Kochanek K. Phototherapy and photochemotherapy. Clin Dermatol 2008 Sep;26(5):464-76. [PubMed]

26. Baden HP, Parrington JM, Delhanty JD, et al. DNA synthesis in normal and xeroderma pigmentosum fibroblasts following treatment with 8-methoxypsoralen and long wave ultraviolet light. Biochim Biophys Acta 1972 Mar 24;262(3):247-55. [PubMed]

27. Walter JF, Kelsey WH, Voorhees JJ, et al. Psoralen plus black light inhibits epidermal DNA synthesis. Arch Dermatol 1973 Jun;107(6):861-5. [PubMed]

28. Wenk J, Brenneisen P, Meewes C, et al. UV-induced oxidative stress and photoaging. Curr Probl Dermatol 2001;29:83-94. [PubMed]

29. Kostovic K, Pasic A. Phototherapy of psoriasis: review and update. Acta Dermatovenerol Croat 2004;12(1):42-50. [PubMed]

30. Gonzalez E. PUVA for psoriasis. Dermatol Clin 1995 Oct;13(4):851-66. [PubMed]

31. Fukuyama K, Epstein WL, Epstein JH. Effect of ultraviolet light on RNA and protein synthesis in differentiated epidermal cells. Nature 1967 Dec 9;216(5119):1031-2. [PubMed]

32. Epstein JH, Fukuyama K, Reed WB, et al. Defect in DNA synthesis in skin of patients with xeroderma pigmentosum demonstrated in vivo. Science 1970 Jun 19;168(938):1477-8. [PubMed]

33. Ozawa M, Ferenczi K, Kikuchi T, et al. 312-nanometer ultraviolet B light (narrow-band UVB) induces apoptosis of T cells within psoriatic lesions. J Exp Med 1999 Feb 15;189(4):711-8. [PubMed]

34. Johnson R, Staiano-Coico L, Austin L, et al. PUVA treatment selectively induces a cell cycle block and subsequent apoptosis in human T-lymphocytes. Photochem Photobiol 1996 May;63(5):566-71. [PubMed]

35. Duthie MS, Kimber I, Norval M. The effects of ultraviolet radiation on the human immune system. Br J Dermatol 1999 Jun;140(6):995-1009. [PubMed]

36. Nickoloff BJ. Cracking the cytokine code in psoriasis. Nat Med 2007 Mar;13(3):242-4. [PubMed]

37. Sethi G, Sodhi A. Role of p38 mitogen-activated protein kinase and caspases in UV-B-induced apoptosis of murine peritoneal macrophages. Photochem Photobiol 2004 Jan;79(1):48-54. [PubMed]

38. Krutmann J, Khan IU, Wallis RS, et al. Cell membrane is a major locus for ultraviolet B-induced alterations in accessory cells. J Clin Invest 1990 May;85(5):1529-36. [PubMed]

39. Simon JC, Krutmann J, Elmets CA, et al. Ultraviolet B-irradiated antigen-presenting cells display altered accessory signaling for T-cell activation: relevance to immune responses initiated in skin. J Invest Dermatol 1992 Jun;98(6 Suppl):66S-9S. [PubMed]

40. Krueger GG, Feldman SR, Camisa C, et al. Two considerations for patients with psoriasis and their clinicians: what defines mild, moderate, and severe psoriasis? What constitutes a clinically significant improvement when treating psoriasis? J Am Acad Dermatol 2000 Aug;43(2 Pt 1):281-5. [PubMed]

41. Pariser DM, Bagel J, Gelfand JM, et al. National Psoriasis Foundation clinical consensus on disease severity. Arch Dermatol 2007 Feb;143(2):239-42. [PubMed]

42. Lebwohl M. A clinician's paradigm in the treatment of psoriasis. J Am Acad Dermatol 2005 Jul;53(1 Suppl 1):S59-S69. [PubMed]

43. Adrian RM, Parrish JA, Momtaz T, et al. Outpatient phototherapy for psoriasis. Arch Dermatol 1981 Oct;117(10):623-6. [PubMed]

44. LeVine MJ, Parrish JA. Outpatient phototherapy of psoriasis. Arch Dermatol 1980 May;116(5):552-4. [PubMed]

45. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 5. Guidelines of care for the treatment of psoriasis with phototherapy and photochemotherapy. J Am Acad Dermatol 2010 Jan;62(1):114-35. [PubMed]

46. Coven TR, Burack LH, Gilleaudeau R, et al. Narrowband UV-B produces superior clinical and histopathological resolution of moderate-to-severe psoriasis in patients compared with broadband UV-B. Arch Dermatol 1997 Dec;133(12):1514-22. [PubMed]

47. Walters IB, Burack LH, Coven TR, et al. Suberythemogenic narrow-band UVB is markedly more effective than conventional UVB in treatment of psoriasis vulgaris. J Am Acad Dermatol 1999 Jun;40(6 Pt 1):893-900. [PubMed]

48. Larko O. Treatment of psoriasis with a new UVB-lamp. Acta Derm Venereol 1989;69(4):357-9. [PubMed]

49. Henseler T, Wolff K, Honigsmann H, et al. Oral 8-methoxypsoralen photochemotherapy of psoriasis. The European PUVA study: a cooperative study among 18 European centres. Lancet 1981 Apr 18;1(8225):853-7. [PubMed]

50. Melski JW, Tanenbaum L, Parrish JA, et al. Oral methoxsalen photochemotherapy for the treatment of psoriasis: a cooperative clinical trial. J Invest Dermatol 1977 Jun;68(6):328-35. [PubMed]

51. Spuls PI, Witkamp L, Bossuyt PM, et al. A systematic review of five systemic treatments for severe psoriasis. Br J Dermatol 1997 Dec;137(6):943-9. [PubMed]

52. Griffiths CE, Clark CM, Chalmers RJ, et al. A systematic review of treatments for severe psoriasis. Health Technol Assess 2000;4(40):1-125. [PubMed]

53. Matz H. Phototherapy for psoriasis: what to choose and how to use: facts and controversies. Clin Dermatol 2010 Jan;28(1):73-80. [PubMed]

54. Stern RS. Genital tumors among men with psoriasis exposed to psoralens and ultraviolet A radiation (PUVA) and ultraviolet B radiation. The Photochemotherapy Follow-up Study. N Engl J Med 1990 Apr 19;322(16):1093-7. [PubMed]

55. Morison WL, Baughman RD, Day RM, et al. Consensus workshop on the toxic effects of long-term PUVA therapy. Arch Dermatol 1998 May;134(5):595-8. [PubMed]

56. Stern RS, Laird N. The carcinogenic risk of treatments for severe psoriasis. Photochemotherapy Follow-up Study. Cancer 1994 Jun 1;73(11):2759-64. [PubMed]

57. Lee E, Koo J, Berger T. UVB phototherapy and skin cancer risk: a review of the literature. Int J Dermatol 2005 May;44(5):355-60. [PubMed]

58. Hearn RM, Kerr AC, Rahim KF, et al. Incidence of skin cancers in 3867 patients treated with narrow-band ultraviolet B phototherapy. Br J Dermatol 2008 Sep;159(4):931-5. [PubMed]

59. Stern RS, Thibodeau LA, Kleinerman RA, et al. Risk of cutaneous carcinoma in patients treated with oral methoxsalen photochemotherapy for psoriasis. N Engl J Med 1979 Apr 12;300(15):809-13. [PubMed]

60. Stern RS, Laird N, Melski J, et al. Cutaneous squamous-cell carcinoma in patients treated with PUVA. N Engl J Med 1984 May 3;310(18):1156-61. [PubMed]

61. Nijsten TE, Stern RS. The increased risk of skin cancer is persistent after discontinuation of psoralen+ultraviolet A: a cohort study. J Invest Dermatol 2003 Aug;121(2):252-8. [PubMed]

62. Lindelof B, Sigurgeirsson B, Tegner E, et al. PUVA and cancer risk: the Swedish follow-up study. Br J Dermatol 1999 Jul;141(1):108-12. [PubMed]

63. Murase JE, Lee EE, Koo J. Effect of ethnicity on the risk of developing nonmelanoma skin cancer following long-term PUVA therapy. Int J Dermatol 2005 Dec;44(12):1016-21. [PubMed]

64. Feldman SR, Fleischer AB, Jr., Reboussin DM, et al. The economic impact of psoriasis increases with psoriasis severity. J Am Acad Dermatol 1997 Oct;37(4):564-9. [PubMed]

65. Miller DW, Feldman SR. Cost-effectiveness of moderate-to-severe psoriasis treatment. Expert Opin Pharmacother 2006 Feb;7(2):157-67. [PubMed]

66. Feldman SR, Garton R, Averett W, et al. Strategy to manage the treatment of severe psoriasis: considerations of efficacy, safety and cost. Expert Opin Pharmacother 2003 Sep;4(9):1525-33. [PubMed]

67. Zanolli MD. Phototherapy treatment protocols : for psoriasis and other phototherapy responsive dermatoses. London ; New York: Taylor & Francis, 2005.

68. van WH, Baart de la FH, Young E, et al. Comparison of narrow-band UV-B phototherapy and PUVA photochemotherapy in the treatment of psoriasis. Acta Derm Venereol 1990;70(3):212-5. [PubMed]

69. Tanew A, Radakovic-Fijan S, Schemper M, et al. Narrowband UV-B phototherapy vs photochemotherapy in the treatment of chronic plaque-type psoriasis: a paired comparison study. Arch Dermatol 1999 May;135(5):519-24. [PubMed]

70. Markham T, Rogers S, Collins P. Narrowband UV-B (TL-01) phototherapy vs oral 8-methoxypsoralen psoralen-UV-A for the treatment of chronic plaque psoriasis. Arch Dermatol 2003 Mar;139(3):325-8. [PubMed]

71. Gordon PM, Diffey BL, Matthews JN, et al. A randomized comparison of narrow-band TL-01 phototherapy and PUVA photochemotherapy for psoriasis. J Am Acad Dermatol 1999 Nov;41(5 Pt 1):728-32. [PubMed]

72. Yones SS, Palmer RA, Garibaldinos TT, et al. Randomized double-blind trial of the treatment of chronic plaque psoriasis: efficacy of psoralen-UV-A therapy vs narrowband UV-B therapy. Arch Dermatol 2006 Jul;142(7):836-42. [PubMed]

73. Cripps DJ, Lowe NJ. Photochemotherapy for psoriasis remission times. Psoralens and UV-A and combined photochemotherapy with anthralin. Clin Exp Dermatol 1979 Dec;4(4):477-83. [PubMed]

74. Housman TS, Rohrback JM, Fleischer AB, Jr., et al. Phototherapy utilization for psoriasis is declining in the United States. J Am Acad Dermatol 2002 Apr;46(4):557-9. [PubMed]

75. Nijsten T, Rolstad T, Feldman SR, et al. Members of the national psoriasis foundation: more extensive disease and better informed about treatment options. Arch Dermatol 2005 Jan;141(1):19-26. [PubMed]

76. Simpson GL, Yelverton CB, Rittenberg S, et al. Do utilization management controls for phototherapy increase the prescription of biologics? J Dermatolog Treat 2006;17(6):359-61. [PubMed]

77. Naldi L, Griffiths CE. Traditional therapies in the management of moderate to severe chronic plaque psoriasis: an assessment of the benefits and risks. Br J Dermatol 2005 Apr;152(4):597-615. [PubMed]

78. Yentzer BA, Yelverton CB, Simpson GL, et al. Paradoxical effects of cost reduction measures in managed care systems for treatment of severe psoriasis. Dermatol Online J 2009;15(4):1. [PubMed]

79. Koek MB, Buskens E, Bruijnzeel-Koomen CA, et al. Home ultraviolet B phototherapy for psoriasis: discrepancy between literature, guidelines, general opinions and actual use. Results of a literature review, a web search, and a questionnaire among dermatologists. Br J Dermatol 2006 Apr;154(4):701-11. [PubMed]

80. Sarkany RP, Anstey A, Diffey BL, et al. Home phototherapy: report on a workshop of the British Photodermatology Group, December 1996. Br J Dermatol 1999 Feb;140(2):195-9. [PubMed]

81. Murphy GM, McCann P, O'Leary A, et al. Guidelines for the use of phototherapy and photochemotherapy in Ireland. Ir J Med Sci 1997 Apr;166(2):92-7. [PubMed]

82. Guidelines of care for phototherapy and photochemotherapy. American Academy of Dermatology Committee on Guidelines of Care. J Am Acad Dermatol 1994 Oct;31(4):643-8. [PubMed]

83. Guidelines of care for psoriasis. Committee on Guidelines of Care. Task Force on Psoriasis. J Am Acad Dermatol 1993 Apr;28(4):632-7. [PubMed]

84. Yelverton CB, Yentzer BA, Clark A, et al. Home narrowband UV-B phototherapy in combination with low-dose acitretin in patients with moderate to severe psoriasis. Arch Dermatol 2008 Sep;144(9):1224-5. [PubMed]

85. Nolan BV, Yentzer BA, Feldman SR. A review of home phototherapy for psoriasis. Dermatol Online J 2010;16(2):1. [PubMed]

86. Haykal KA, DesGroseilliers JP. Are narrow-band ultraviolet B home units a viable option for continuous or maintenance therapy of photoresponsive diseases? J Cutan Med Surg 2006 Sep;10(5):234-40. [PubMed]

87. Koek MB, Sigurdsson V, van WH, et al. Cost effectiveness of home ultraviolet B phototherapy for psoriasis: economic evaluation of a randomised controlled trial (PLUTO study). BMJ 2010;340:c1490. [PubMed]

88. Yelverton CB, Kulkarni AS, Balkrishnan R, et al. Home ultraviolet B phototherapy: a cost-effective option for severe psoriasis. Manag Care Interface 2006 Jan;19(1):33-6, 39. [PubMed]

89. Yelverton CB, Balkrishnan R, Feldman SR. The utility of a data-

logging device for measuring adherence to home phototherapy. Photodermatol Photoimmunol Photomed 2006 Oct;22(5):270-2. [PubMed]

90. Yentzer BA, Yelverton CB, Pearce DJ, et al. Adherence to acitretin and home narrowband ultraviolet B phototherapy in patients with psoriasis. J Am Acad Dermatol 2008 Oct;59(4):577-81. [PubMed]

91. National Biological Corp. UV Phototherapy is a Safe, Effective, and Economical Psoriasis Treatment. 2010 [cited 2010 May 1]

92. National Psoriasis Foundation. Treating psoriasis Moderate to severe psoriasis: Home UVB equipment. 2010 [cited 2010 May 1]

93. The Daalvin Company. Phototherapy Units for Home Use. 2010 [cited 2010 May 1];]

94. UVBioTek. Home Phototherapy Equipment. 2010 [cited 2010 May 1]

95. Solarc Systems. Home UVB Phototherapy Selection Guide. 2010 [cited 2010 May 1]

96. Psoralite. Home Equipment Psoralite Corporation. 2010 [cited 2010 May 1]

97. Richmond Light. Home Phototherapy Products. 2010 [cited 2010 May 1]

98. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. Arch Dermatol 1988 Jun;124(6):869-71. [PubMed]

99. Zanolli M. Phototherapy arsenal in the treatment of psoriasis. Dermatol Clin 2004 Oct;22(4):397-406, viii. [PubMed]

100. Valkova S. UVB phototherapeutic modalities. Comparison of two treatments for chronic plaque psoriasis. Acta Dermatovenerol Alp Panonica Adriat 2007 Mar;16(1):26-30. [PubMed]

101. Kleinpenning MM, Smits T, Boezeman J, et al. Narrowband ultraviolet B therapy in psoriasis: randomized double-blind comparison of high-dose and low-dose irradiation regimens. Br J Dermatol 2009 Dec;161(6):1351-6. [PubMed]

102. Boztepe G, Akinci H, Sahin S, et al. In search of an optimum dose escalation for narrowband UVB phototherapy: is it time to quit 20% increments? J Am Acad Dermatol 2006 Aug;55(2):269-71. [PubMed]

103. Ibbotson SH, Bilsland D, Cox NH, et al. An update and guidance on narrowband ultraviolet B phototherapy: a British Photodermatology Group Workshop Report. Br J Dermatol 2004 Aug;151(2):283-97. [PubMed]

104. Wainwright NJ, Dawe RS, Ferguson J. Narrowband ultraviolet B (TL-01) phototherapy for psoriasis: which incremental regimen? Br J Dermatol 1998 Sep;139(3):410-4. [PubMed]

105. Honigsmann H. Phototherapy for psoriasis. Clin Exp Dermatol

2001 Jun;26(4):343-50. [PubMed]