

# The utilization of phototherapy in the department of dermatology, Hospital Kuala Lumpur: A 5-year audit

Vaani Valerie Visuvanathan, AdvMDerm<sup>1</sup>, Min Moon Tang, AdvMDerm<sup>2</sup>, Li Lian Tan, MRCP<sup>2</sup>, Asmah Johar, MMed<sup>2</sup>

<sup>1</sup>Clinical School, International Medical University, Seremban, Negeri Sembilan, Malaysia, <sup>2</sup>Department of Dermatology, Hospital Kuala Lumpur, Malaysia

## ABSTRACT

**Introduction:** Ultraviolet phototherapies are important treatment modalities for a wide range of dermatological conditions. We aim to describe the utilization of phototherapy in the Department of Dermatology Hospital Kuala Lumpur.

**Methods:** This is a 5-year retrospective audit on patients who underwent phototherapy between 2011 and 2015.

**Results:** There were 892 patients, M:F=1.08:1, aged from 4-88 years, with a median age of 38.8 years who underwent phototherapy. Majority (58.9%) had skin phototype IV, followed by type III (37.7%) and type II (0.7%). There were 697(78.1%) who underwent NBUVB, 136 (15.2%) had topical PUVA, 22(2.5%) had oral PUVA, 12(1.4%) had UVA1 and 23(2.6%) had NBUVB with topical or oral PUVA/UVA1 at different time periods. The indications were psoriasis (46.6%), vitiligo (26.7%), atopic eczema (9.8%), pityriasis lichenoides chronica (5.3%), mycosis fungoides (3.9%), lichen planus (2.5%), nodular prurigo (2.2%), scleroderma (1.2%), alopecia areata (0.7%) and others. The median number of session received were 27 (range 1-252) for NBUVB, 30 (range 1-330) for topical PUVA, 30 (range 3-190) for oral PUVA and 24.5 (range 2-161) for UVA1. The acute adverse effects experienced by patients were erythema (18%), pruritus (16.3%), warmth (3.3%), blister formation (3.1%), cutaneous pain (2.4%), and xerosis (0.8%), skin swelling (0.7%) and phototoxicity (0.2%).

**Conclusion:** Narrow-band UVB was the most frequently prescribed phototherapy modality in our center. The most common indication for phototherapy in our setting was psoriasis. Acute adverse events occurred in a third of patients, although these side effects were mild.

## KEY WORDS:

Phototherapy, UVB, PUVA, psoriasis, eczema

## INTRODUCTION

Phototherapy has been a useful treatment modality administered almost exclusively by dermatologist since the 19th century when Niels Finsen was awarded the Nobel prize (1903) for successfully treating lupus vulgaris using carbon arc light source. However, the usage of phototherapy can be dated back to 1400BC by the Indians and Egyptians using the

pigment-stimulating properties of the psoralen-containing Bavachee plant (*Psoralea corylifolia*) and *Ammi majus* respectively for the treatment of vitiligo.<sup>1,2</sup> In current times, phototherapy and photochemotherapy play a significant role in the treatment of various dermatological disorders including chronic plaque psoriasis, atopic dermatitis, vitiligo, alopecia areata, cutaneous T-cell lymphoma, graft versus host disease, lichen planus, pityriasis lichenoides chronica, polymorphous light eruption and pityriasis rubra pilaris.<sup>1</sup>

Phototherapy services have been established in Department of Dermatology, Hospital Kuala Lumpur since 1984, offering ultraviolet A (UVA) and broad-band based ultraviolet B (BBUVB) and later providing Narrow-band ultraviolet B (NB-UVB) in 2003.<sup>3</sup> The department currently has two units of Daavlin cabin (UVA and NBUVB), a hands and feet unit, two Dermalight handheld (NBUVB and UVA), two NBUVB combs, a localized unit of UVA1 and a localized unit of Waldmann (UVA and UVB).

The objective of this audit was to describe the utilization of phototherapy particularly on the indications for therapy, types of phototherapy prescribed and documented acute side effects.

## METHODOLOGY

This is a retrospective audit on all patients who had received phototherapy or photochemotherapy between 2011 and 2015 in Hospital Kuala Lumpur. Data was collected from the phototherapy folders and medical records of the patients. Patients' demographic characteristics, types of phototherapy received, the indications and the acute side effects were captured. Data was then analyzed using SPSS®13.0.

## RESULTS

A total of 892 patients received either one or more types of phototherapy between 2011 and 2015. The demographic data was shown in Table I. The gender distribution of patients is almost equal with 52% (n=464) of patients being males and 48% (n=428) females. As a representation of the population, majority of patients had skin phototype III and IV. Over this five year period, 74 children had undergone phototherapy, with the ages ranging between 4 and 16 years. The mean age for children who had received NBUVB and topical PUVA was 13.2 years and 11.8 years respectively.

This article was accepted: 4 April 2018

Corresponding Author: Vaani Valerie Visuvanathan

Email: vaani\_valerie@imu.edu.my

**Table I: Demographic and treatment characteristics of patients in Hospital Kuala Lumpur**

Parameters	Total N=892	Adult N=818	Paediatric N=74
Mean age years (range)	38.8 (4-88 )	41.2 (17-88)	12.7 (4-16)
Gender, n (%)			
Male	464 (52)	426 (50)	38 (51)
Female	428 (48)	392 (50)	36 (49)
Fitzpatrick skin phototype, n (%)			
Type I	1 (0.1)	1(0.12)	0.
Type II	6 (0.7)	6(0.73)	0
Type III	337 (37.8)	317(38.8)	20(27)
Type IV	525 (58.9)	475(58.1)	54(73).
Type V	1 (0.1)	1(0.12)	0
Phototherapy modality prescribed, n (%)			
NBUVB	713 (80.0)	665 (81.3)	48(64.9)
Topical / bath PUVA	141 (15.8)	116 (14.2)	25(33.8)
Oral PUVA	23 (2.6)	23 (2.8)	0
UVA1	13 (1.4)	12 (1.5)	1(1.3)
NBUVB + psoralen	2 (0.2)	2 (0.2)	0
Patients who had required more than 1 modality of phototherapy			
Topical PUVA – NBUVB	5	2	3
NBUVB – topical PUVA	13	13	0
NBUVB – oral PUVA	2	2	0
NBUVB – UVA1	1	1	0

Paediatric – those less than 17 years

**Table II: Indications for phototherapy and the side effects experienced among patients in Hospital Kuala Lumpur**

Indications	Total n=892 (%)	Adult n=818 (%)	Paediatric n=74 (%)
Psoriasis	416 (46.6)	399 (48.8)	17 (23.0)
Vitiligo	238 (26.7)	206 (25.2)	32 (43.2)
Atopic eczema	87 (9.8)	79(9.7)	8(10.8)
Pityriasis lichenoides chronica	47 (5.3)	39(4.8)	8(10.8)
Mycosis fungoides	35 (3.9)	29(3.5)	6(8.1)
Lichen planus	22 (2.5)	22(2.7)	-
Nodular prurigo	20 (2.2)	20(2.4)	-
Scleroderma	11 (1.2)	10(1.2)	1(1.4)
Alopecia areata - totalis	6 (0.7)	5(0.6)	1(1.4)
Chronic actinic dermatitis	2 (0.2)	2(0.2)	-
Idiopathic guttate hypomelanosis	2 (0.2)	2(0.2)	-
Perforating collagenosis	1 (0.1)	1(0.1)	-
Erythroderma	1 (0.1)	1(0.1)	-
Pretibial myxedema	1 (0.1)	1(0.1)	-
Pityriasis alba	1 (0.1)	-	1(1.4)
<b>Side effects</b>	<b>n(%)</b>	<b>n(%)</b>	<b>n(%)</b>
Erythema	155 (17.4)	142(17.4)	13(17.6)
Pruritus	141 (15.8)	135(16.5)	6(8.1)
Increased warmth	29 (3.3)	28(3.4)	1(1.4)
Blistering	24 (2.7)	20(2.4)	4(5.4)
Cutaneous pain	21 (2.4)	21(2.6)	-
Oedema	6 (0.7)	6(0.7)	-
Xerosis	4 (0.4)	5(0.6)	-
Phototoxicity	2 (0.2)	1(0.1)	1(1.4)

Paediatric – those less than 17 years

**Table III: Indications and prescribing pattern of phototherapy in Hospital Kuala Lumpur in comparison to other centers**

Author, year	Country	Types of phototherapy	Indications (%)							
			Psoriasis	Vitiligo	AD	CTCL	Scleroderma	PLC	AA	Others
Park et al, 1996	Korea	PUVA	28.0	70.2	0.5	0.5	-	-	-	0.7
		UVB	94.8	-	2.4	-	-	-	-	2.9
Huynh et al 2002	Australia	PUVA	9.4	9.4	6.7	11.5	0.8	4.8	5.3	46.0
		NBUVB	12.1	6.0	11.4	5.8	0.1	10.8	0.8	46.7
Duarte et al, 2009	Brazil	PUVA	23.9	-	-	-	-	-	-	-
		NBUVB	76.1	-	-	-	-	-	-	-
Current study, 2017	Malaysia	Oral PUVA	17.4	21.7	4.3	47.8	4.3	4.3	-	-
		Topical PUVA	2.8	85.1	1.4	0.7	1.4	3.5	3.5	1.4
		NBUVB	57.2	15.4	11.4	3.2	-	5.6	0.1	7.1
		UVA1	-	7.7	23.1	-	61.5	7.7	-	-

AA – alopecia areata  
 AD – atopic dermatitis  
 CTCL – cutaneous T-cell lymphoma  
 PLC – pityriasis lichenoides chronica

**Table IV: Adverse events from phototherapy at 3 different centers**

	Tuchinda et al, 2006	Martin et al 2007			Current study 2017				
	United States	United Kingdom			Malaysia				
Phototherapy modality	UVA1	Oral PUVA	Top PUVA	NBUVB	Oral PUVA	Top PUVA	NBUVB	UVA1	NBUVB + Psoralen
Number of patients	92	299	2511	5974	23	141	713	13	2
Acute adverse event (%)	15	1.6	2.1	0.6	31	53	30	8	0
Common adverse events (%)	Erythema Pruritus Tender	Erythema			Erythema (26) Pruritus (9)	Erythema (37) Blister Pruritus (11)	Pruritus (17) Erythema (14)	Erythema (8)	-

**Table V: Data regarding phototherapy among children in Hospital Kuala Lumpur, UK and New Zealand**

Type of phototherapy	Jury et al 2006, UK	Tan et al, 2010 New Zealand	Current study, 2017 Hospital Kuala Lumpur		
	NBUVB	NBUVB	NBUVB	Topical PUVA	UVA1
Number of patients	77	116	48	25	1
Mean age in years (Range)	12 (4-16)	11 (2.6-15.9)	13.2 (4-16)	11.8 (5-16)	15
M:F	1:1.8	1.3:1	1:1.3	1	-
Skin photo-type (%)	I	-	4.9	-	-
	II	-	50.0	-	-
	III	-	25.0	31.2	16.0
	IV	-	19.4	68.8	84.0
	IV	-	0.7	-	-
Indications (%)	Psoriasis (45) AD (32)	AD (53) Psoriasis (33) PLC (3)	Psoriasis (35) Vitiligo (21) AD (8)	Vitiligo (21) PLC (8) Alopecia (4)	Scleroderma
Side effects (%)	Erythema Herpes reactivation	Erythema(31)	Pruritus(8)	Erythema(40)	Erythema

AD – atopic dermatitis  
 PLC – pityriasis lichenoides chronica

The most commonly prescribed type of phototherapy was NBUBV, followed by bath or topical PUVA and together represented more than 90% of treatment. The median number of NBUBV sessions received by patients was 27 sessions, with a maximum of 252 sessions. The number of topical and oral PUVA sessions ranged between 1-330 sessions and 3-190 sessions respectively. Twenty three patients received NBUBV and later changed to topical or bath PUVA as a second line treatment agent or vice versa. Oral PUVA and UVA1 were prescribed to 22 (2.5%) and 12 (1.4%) patients respectively. For the paediatric age group, the maximum number of topical PUVA and NBUBV prescribed was 330 and 177 sessions respectively.

As shown in Table II, the primary indication for phototherapy was psoriasis, prescribed for 416 patients (46.6%). Vitiligo was the second most common diagnosis among those who had been prescribed phototherapy and half of these patients (n=120) had undergone topical PUVA (Table III). About 10% of patients had received phototherapy as a therapeutic option for atopic eczema and NBUBV was prescribed for most of them (93.1%). Pityriasis lichenoides chronica, mycosis fungoides, lichen planus and nodular prurigo were some of the other indications for phototherapy and again NBUBV being the preferred modality of treatment. Eleven patients with scleroderma had been prescribed phototherapy and eight of them had received UVA1. Of the remaining three patients with scleroderma, two had received topical PUVA and one underwent oral PUVA. Among the paediatric age group, psoriasis, vitiligo and atopic dermatitis were the common indications for phototherapy.

One third of patients who received phototherapy experienced adverse effects, majority of which were mild and did not result in treatment interruption. Forty-one patients (4.6%) were withdrawn from treatment due to severe or intolerable adverse events. As shown in Table IV, the highest rate of adverse effects was noted in patients who received topical and bath PUVA (53%). The rates of adverse effects for NBUBV and oral PUVA were about 30% for both treatment modalities. Erythema and pruritus were the two most common adverse effects, with an incidence of 17.3% and 15.8% respectively (Table II). Pruritus was the adverse effect which occurred more frequently among patients who received NBUBV while erythema was more frequent among those who received PUVA and UVA1 (Table IV). Most children tolerated phototherapy well. Pruritus was experienced by 16.7% of children who underwent NBUBV whereas erythema was the most common side effect reported by those who were prescribed Topical PUVA and UVA1.

## DISCUSSION

Phototherapy can be administered by dermatologists in the form of PUVA photochemotherapy (the use of psoralen and long-wave UVA radiation, 320 to 400 nm), UVA1 (340 to 400 nm), broadband UVB therapy (290 to 320 nm), narrowband UVB (311-312 nm), Excimer 308 nm UVB light, extracorporeal photopheresis (320-400nm), heliotherapy and photodynamic therapy.<sup>1,4</sup> Ultraviolet light B radiation primarily acts on cells at the epidermis and the epidermo-

dermal junction, whereas UVA radiation affects epidermal and dermal components, especially dermal blood vessels.<sup>4</sup>

Narrow band UVB is often preferred and prescribed more frequently than PUVA, especially for the treatment of psoriasis. This may be due to the perceived increased in carcinogenic risk associated with PUVA and the better safety profile of NBUBV. Although UV light generally has a carcinogenic potential, till now there is no solid evidence of increased skin cancer risk in psoriasis patients treated with either BBUBV or NBUBV phototherapy.<sup>5</sup> However, PUVA in high doses substantially increases the risk of squamous cell carcinoma and melanoma.<sup>6</sup> Moreover, patients on NBUBV do not require the usage of eye protection post treatment and it can be utilized by pregnant females and children.

Interestingly, there were two patients with vitiligo who were prescribed a combination of topical psoralen and NBUBV. One of them had five sessions of localized NBUBV administered via handheld device whilst the other patient had underwent 22 sessions of NBUBV via a cabin. Both patients responded well to therapy with no recorded side effects. The efficacy and mechanism of action of psoralen and NBUBV combination is not well established in the treatment of vitiligo. However, in a study by de Berker et al., oral psoralen and NBUBV combination was found to be as effective as PUVA to achieve clearance in patients with plaque psoriasis, with patients requiring lower cumulative doses for clearance.<sup>7</sup>

Generally lacking systemic toxicities with well-known side effects and good outcome, phototherapy is one of the superheroes in the dermatologist's armamentarium despite the arrival of biologics. The requirement to be present at the healthcare center on two or three days in a week can be daunting for most patients. Phototherapy may not be readily accessible for some patients, as the service is not offered in all hospitals. In addition to these challenges, the cost for phototherapy is not covered by health insurance despite the reduced work time which leads to loss of income, and the long term side effects of phototherapy that are not clearly understood.

The prescribing patterns of phototherapy in various countries are shown in Table III. In a study by Park SH et al., who analyzed the protocols for phototherapy among patients who received phototherapy in Yonsei Medical Centre, Korea over a ten-year period, vitiligo was the main indication for oral and topical PUVA therapy, whereas the majority of patients who underwent UVB had psoriasis.<sup>8</sup> A questionnaire-based survey involving 112 dermatologists in Australia, revealed that 98% of dermatological phototherapists used UVB.<sup>9</sup> Psoralen and UVA (oral and topical) was chosen by most dermatologists for treatment of vitiligo, alopecia areata, alopecia totalis, cutaneous T-cell lymphoma and chronic actinic dermatitis while NBUBV was preferred for the treatment of atopic dermatitis, pruritus, pityriasis lichenoides and eosinophilic folliculitis.<sup>9</sup> Duarte et al. studied the prescription behaviour for 67 patients with psoriasis who underwent phototherapy in two medical centres in Sao Paulo, Brazil, and noted that 51 patients (76%) were treated with NBUBV.<sup>10</sup> The studies done in Korea and Australia suggest

that majority of patients with vitiligo are prescribed UVA phototherapy, this differs from the finding in Hospital Kuala Lumpur where prescription of UVA and UVB for patients with vitiligo was of almost equal number.

Literature regarding the use of phototherapy in children is rather limited. There is also a paucity of long-term safety data of phototherapy and photochemotherapy in children. Phototherapy among children can be challenging due to various factors, including time commitments of the family, accessibility, safety concerns due to unclear long term side effects, child's anxiety and difficulty in ensuring proper eye protection. The age for initiation of phototherapy depends on the type of phototherapy and is based on conventional wisdom rather than guidelines. The child's behavioral development and temperament should be assessed, including separation anxiety, fear of enclosed spaces, and ability to remain still during treatments prior to initiation of phototherapy. Some children may be more comfortable if accompanied by a parent or care giver during the first few sessions of phototherapy. Narrow-band UVB is often preferably prescribed for children. It is proposed that the maximum duration of NBUBV phototherapy in children should be 12 months. If NBUBV is required for a longer period, targeted phototherapy is proposed.<sup>11</sup> Concerns regarding development of cataract, have led to recommendations that PUVA should not be prescribed to children below 10 years of age.

Jury et al. who undertook a retrospective review on the use of NBUBV in a pediatric population attending two Glasgow Hospitals noted that in children, the conditions most commonly treated by phototherapy are psoriasis and atopic dermatitis.<sup>12</sup> The adverse event profile was similar to that in adults, with erythema (30.0%), blistering (6.5%) and herpes simplex reactivation (2.6%). The mean age of children in the population was 12 years. A prospective analysis of children who had received NBUBV phototherapy over a fifteen-year period at a tertiary center in New Zealand revealed that the main indication for phototherapy was atopic dermatitis followed by psoriasis, pityriasis lichenoides, nodular prurigo, morphea, vitiligo, urticaria pigmentosa and erythropoietic porphyria.<sup>13</sup> The mean age of the children was 11.0 years. Mild erythema (36%) was the most commonly reported side effect. The mean age of children who underwent NBUBV in our center was similar compared to the above mentioned studies. The indications were also similar, psoriasis, atopic dermatitis and vitiligo being the more common indications. However, majority of children who were prescribed NBUBV in our cohort experienced pruritus as a side effect, whereas data from the other two centers described erythema as the more common side effect. This may be due to the difference in skin phototype among the population and also the difference in phototherapy protocol.

Despite its versatility in the management of numerous dermatological conditions, phototherapy is accompanied by adverse effects, which may be acute, when occurring immediately up to six weeks after therapy i.e. erythema, xerosis, pruritus, blistering, increased frequency of recurrent herpes simplex viral infections and photoconjunctivitis. Chronic adverse events are those which are encountered six

weeks or more after therapy and these include pigmentary disorders, photoaging, cataracts and carcinogenesis.<sup>14</sup> Adverse events from phototherapy as had been described in studies from the United States and the United Kingdom is depicted in Table V. In a retrospective study which looked at data collected from 92 patients of UVA1-treated cutaneous conditions from four medical centers in the United States in 2006, about 15% of patients experienced minor side effects such as erythema (7.5%) and pruritus (3.2%).<sup>15</sup> Only one patient developed polymorphous light eruption (PMLE) and hence warranted withdrawal from phototherapy. In 2007, Martin et al. published a retrospective study which determined the rate of acute adverse events experienced by patients from three dermatology units in South East Wales.<sup>16</sup> The rate of acute adverse events recorded for all phototherapy treatments was 0.8% and erythema was most commonly reported. Severe adverse events were noted among 4 patients (0.05%). Narrow-band UVB had the lowest rate of acute adverse events (0.6%), and the highest rate was seen with both bath and oral PUVA (1.3%). In our center, the rate of adverse events reported for UVA1 is about half of that reported by Tuchinda et al. whereas the rate for NBUBV and PUVA is significantly higher as compared to the study in South East Wales. This may be due to reporting variability and also the difference in population skin phototype. At our center, the minimal erythema dose (MED) for NBUBV is estimated based on skin phototype of patients with dosage increments of 25% at each treatment. In the study by Martin et al, the MED of every patient was established prior to therapy and followed a dosing increment of 20% at each subsequent treatment in the absence of erythema. This variation in protocol and higher increment rates could possibly account for the higher adverse event rate recorded at our center. In the future, modification of protocol should be considered where MED has to be established for every patient prior to initiating NBUBV therapy and lower rate of dosing increment.

Phototherapy is a very important treatment option of psoriasis as the efficacy of phototherapy is compatible with other systemic agents. It is an alternative for patients who have failed or contraindicated for other systemic therapies. A course of NBUBV can achieve clearance in 63%-80% of patients with psoriasis.<sup>17</sup> This is considered very good efficacy in comparison with systemic drugs and even with biologics. A retrospective data analysis of psoriasis registry in Austria showed a superior effect of PUVA even over certain biologics (adalimumab, alefacept, efalizumab, etanercept).<sup>18</sup> Phototherapy and methotrexate were also noted to be the most cost-effective therapies for the treatment of severe psoriasis.<sup>19</sup> A study by Feldman and colleagues, which used a 75% improvement in Psoriasis Area and Severity Index (PASI-75) scores as a measure of treatment success, found that methotrexate is the most cost-effective treatment, whereas alefacept has the highest cost per treatment success.<sup>20</sup> Nevertheless, when they factored in considerations of safety, the authors suggested UV-B phototherapy as the first-line agent of choice for severe psoriasis because of the higher risk profile of methotrexate. A study by Beyer and Wolverton estimated a greater than 10-fold difference in cost when comparing biologics to older, traditional treatments, including phototherapy.<sup>21</sup> Hence, the cost of treatment is a

very important determining factor that may dictate the choice of treatment. In a nutshell, phototherapy remains a safe yet very cost-effective treatment for psoriasis.

### CONCLUSION

Narrow-band UVB was the most frequently prescribed phototherapy in our center. The most common indication was psoriasis. Acute adverse events occurred in a third of patients, albeit mild and self-limiting. Phototherapy together with more well-trained dermatological phototherapists should be made available in more healthcare centers. Future studies exploring local data regarding efficacy and long term side effects of phototherapy and photochemotherapy is important in the presence of biologics.

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