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ORIGINAL ARTICLE

Determination of minimal erythema dose of Filipino adults to standardize the initial dose of narrowband ultraviolet B phototherapy in a tertiary hospital

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ABSTRACT

INTRODUCTION Narrowband ultraviolet B (NBUVB) phototherapy is a well-established treatment option for a variety of dermatologic conditions. The initial dosage is obtained either by determining the patients' minimal erythema dose (MED) or their Fitzpatrick skin phototype (SPT). MED determination is a better way to establish the proper initial dose as it is more objective. However, in practice, SPT is more commonly used as it is more convenient, and MED data in Filipinos are scarce.

OBJECTIVES To establish data determining the MED values of Filipino adults that can serve as a basis to standardize the initial dose of NBUVB phototherapy in a tertiary hospital.

METHODS We enrolled 86 volunteers in a cross-sectional analytical study to determine their MED and assess if there is any association between their MED and the participants' age, sex, skin prototype, ancestry, and daily duration of sun exposure.

RESULTS The median MED of the participants is 800 mJ/cm^2 (IQR 600-800 mJ/cm^2). A majority of 38 participants (44.19%) have a MED of 800mJ/cm^2 followed by 600mJ/cm^2 for 23 (26.74%) participants. There was also a significant association between study participants' MED with respect to their Fitzpatrick skin type (p=<0.001) and ancestry (p=0.03), but with no association with regards to age (p=0.291), sex (p=0.245), and daily duration of sun exposure (p=0.237).

CONCLUSION Majority of the participants have a median MED value of 800 mJ/cm^2. Based on this MED value, the initial dosage of NBUVB at 50-70% of the MED would translate to an initial dose of 400-560 mJ/cm^2.

KEYWORDS erythema, phototherapy, minimal erythemus dose

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INTRODUCTION

Phototherapy is the use of ultraviolet (UV) or visible light for therapeutic purposes. One of the most widely used modalities of phototherapy is narrowband UVB (NBUVB). Its beneficial effect is now well established for a variety of dermatologic conditions, as its appeal is based on its relative safety coupled with an ongoing interest in its molecular and biological effects.[1]

The dosage of UV light is prescribed according to the individual's skin sensitivity.[2] There are two ways to determine the initial starting dose of NBUVB. First, the minimal erythema dose (MED) is determined by exposing six square areas of sun-protected skin, each measuring 1 cm^2, to gradually increasing amounts of UV radiation from the same device that will be used for phototherapy. After twenty-four hours, the UV-exposed squares are examined and the lowest UV dose that results in uniform erythema over an entire square is considered the MED; thereafter phototherapy is initiated at 50-70% of that amount. Alternatively, the initial dose of phototherapy may also be established based empirically on Fitzpatrick skin phototype (SPT).[1,2]

In clinical practice, most dermatologists in the Philippines utilize SPT for determining the initial starting dose of NBUVB phototherapy for its practicality and convenience. However, the SPT has limitations as SPT has been shown in studies not to correspond well to constitutive skin color and to correlate poorly with MED values. Interestingly, the physician-assigned skin phototype has been shown to correlate moderately with race,[3,4] and race assignment does not correlate well with objective measures of pigmentation or self-reported skin phototype, suggesting that assignment of SPT is often based

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on perceived race rather than either objective skin color or response to UV light.[4] Hence, administering NBUVB phototherapy solely on the basis of skin type can lead to undertreatment or overdosing of patients particularly in the Filipino population, in whom previous studies regarding MED testing are scarce. Thus, MED determination is a better way to establish the proper initial dose to administer to a patient, thereby enhancing therapeutic efficacy resulting to fewer treatment sessions and less expenses for the patient. The objective of this study is to have data determining the MED values of Filipino adults that can serve as a basis to standardize the initial dose of NBUVB phototherapy in a tertiary hospital.

METHODS

STUDY DESIGN

This is a prospective cross-sectional analytical study conducted in the phototherapy center of a tertiary hospital. This study was approved by the Institutional Review Board prior to commencement.

PATIENT SELECTION AND RECRUITMENT

Subject participants are Filipino citizens, aged 18-60 years old, of both sexes, with no active skin condition that might interfere with the performance of the test or reading of the results, and with no skin lesions in the areas to be tested (hips, lower back, or buttocks) for the MED. Participants with known history of photosensitivity and those who have ingested or applied the following medications within their corresponding time frame: photosensitizing agent within 2 months; corticosteroids within 15 days; and H1-receptor antihistamine within 7 days, from the MED testing were excluded in the study. Eligible participants were informed of the study process and have voluntarily signed the informed consent.

DATA COLLECTION

On the first visit, demographic profile, and the following data: ancestry, Fitzpatrick skin type, and daily duration of sun exposure were taken, and recorded by the primary investigator.

STUDY MATERIALS

Narrowband ultraviolet B (NBUVB) phototherapy device

The medical phototherapy machine (National Biological Corporation) was used for the NBUVB phototherapy sessions. It is a combination phototherapy unit with 24 NBUVB and 24 UVA lamps, measuring 46 x 49 x 87 inches that can treat the whole body in one session.

Minimal erythema dose (MED) test patch

The investigators used the MED (Daavlin®) test patch. It is a disposable hypoallergenic individual test patch comes with six exposure windows for the corresponding doses.

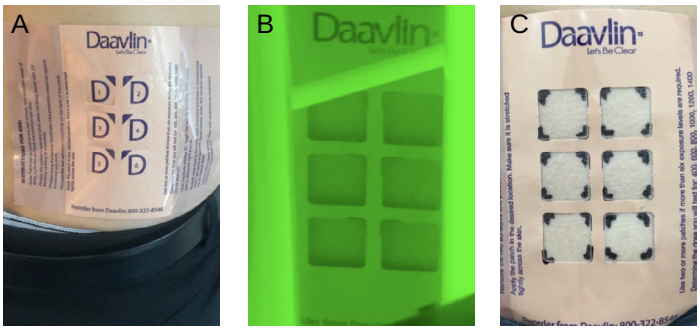

Figure 1. **A.** Attaching the MED test patch on a sun-protected area (lower back), **B.** Conducting UV exposure, **C.** Marking of MED test area.

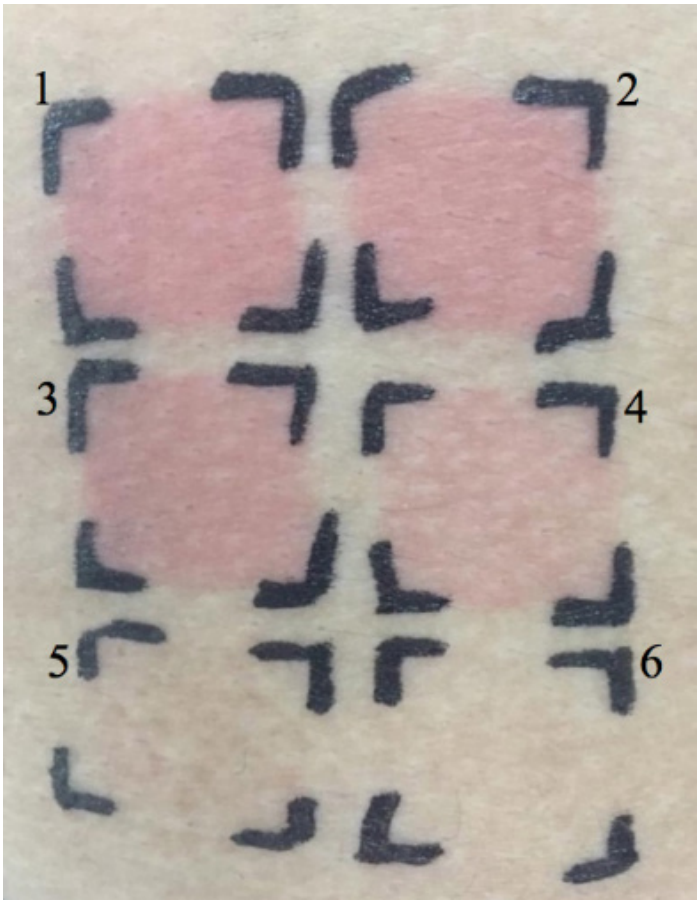

Figure 2. MED reading of a participant showed well defined erythema at square number 4 corresponding to 600mJ/cm^2.

MED TESTING

Preparing for UV exposure

The investigator explained to the participants how MED testing is done, and that the participant has to come back to the center

Table 1. Visual Erythema Scale.

E0	No erythema
E1	Ill-defined erythema (faint pink)
E2	Well defined erythema (pink)
E3	Marked erythema (red)
E4	Fiery red with edema
E5	Fiery red with edema and blistering

for 2 consecutive days for the MED testing and the MED reading. The Daavlin® MED test patch was attached to a sun-protected region of the body, which will either be the hip, lower back or buttocks. All other skin areas were covered using a towel and protective clothing, with eye protection using phototherapy goggles worn during the entire procedure.

Conducting UV exposure

The six squares of the MED test patch were exposed to NBUVB at increasing intervals of 200 mJ/cm^2. At the start of the exposure, only one square of the MED test patch was open, after which an additional square was opened and exposed for every increase in dose exposure.[6] The timer is part of the phototherapy device, which automatically turns the NBUVB lamps off after the desired dose has been reached.

Upon completion of the UV exposure, adequate skin markings using a permanent marker were made prior to the removal of the MED test patch, in order to more easily identify the exposed areas after 24 hours (Figure 1). Participants were reminded to not wash off the markings until after the skin had been examined for the MED reading.

ASSESSING THE MED

The participants had only one follow-up with the principal investigator, which was after 24 hours of the MED testing to determine their MED.

After 24 hours, the investigator examined the exposed areas of skin. Red or pink skin indicated erythema. Well-defined erythematous skin exposed to the shortest duration of NBUVB was defined as the MED (Square number 4 in Figure 2), which will also classify as E2 on the Visual Erythema Scale (Table 1).

ASSESSMENT OF OUTCOME

The primary outcome of interest was the smallest UV dose that resulted in uniform well-defined erythema over the entire exposed area after 24 hours of exposure to the NBUVB light source using a visual erythema scale. The MED was defined as E2 or well-defined erythema (pink) skin in the visual erythema scale. Secondary outcome measures were the participant's subjective assessment of the exposure in terms of pruritus, pain or tenderness using a visual analog scale; and adverse events. These

Table 2. Demographic Profile of the Study participants.

Characteristics	Values (n=86)
Mean age ± SD, years	31.98 + 8.15
Sex, frequency (%)	
Male	30 (34.88)
Female	56 (65.12)
Comorbidity, frequency (%)	
None	71 (82.56)
Hypertension	5 (5.81)
Asthma	7 (8.14)
Allergic rhinitis	1 (1.16)
Endometriosis	1 (1.16)
Hyperthryoidism	1 (1.16)
Allergies, frequency (%)	9 (10.47)
Occupation, frequency (%)	
Healthcare professional	30 (34.88)
Office employee	3 (3.48)
Security personnel	11 (12.79)
Service personnel	40 (46.52)
Others	2 (2.33)
Smoking history, frequency (%)	
Smoker	12 (13.95)
Non smoker	73 (84.88)
Previous smoker	1 (1.16)
Alcohol intake, frequency (%)	
Occasional	55 (63.95)
None	31 (36.05)
Ancestry, frequency (%)	
Pure Filipino	74 (86.05)
Mixed ancestry	
East Asian	8 (9.30)
Mediterranean	4 (4.65)
North European	1 (1.16)
Fitzpatrick skin type, frequency (%)	
Type I	0
Type II	1 (1.16)
Type III	20 (23.26)
Type IV	57 (66.28)
Type V	8 (9.30)
Type VI	0
Daily duration of sun exposure, frequency (%)	
Minimal (less than 10 minutes)	53 (61.63)
Moderate (more than 10minutes, but less than 1 hour)	31 (36.05)
Severe (more than 1 hour)	2 (2.33)

JPDS Journal of the Philippine Dermatological Society

Table 3. Minimal erythema dose, and Subjective assessment of study participants to MED testing.

Characteristics	Frequency (%); Median (IQR)	
Minimal erythema dose (MED) value (mJ/cm²)	800 (600,800)	
200	0	
400	6 (6.98)	
600	23 (26.74)	
800	38 (44.19)	
1,000	13 (15.12)	
1,200	6 (6.98)	
Subjective assessment of study participants to MED testing (Visual Analog Scale 0-10)	**Immediately after MED testing**	**24 hours after MED testing**
Pruritus		
0	86 (100)	82 (95.35)
1	0	0
2	0	2 (2.33)
3	0	2 (2.33)
Pain or tenderness		
0	86 (100)	84 (97.67)
1	0	0
2	0	2 (2.33)
Adverse Effects (Grades 1-3)		
Burning sensation		
0: None	84 (97.67)	
1: Awareness of symptoms but easily tolerated	2 (2.33)	
2: Enough discomfort to cause interference with daily activities	0	
3: Incapacitating with inability to do work	0	

were recorded, and attended to immediately after the MED testing, and after 24 hours of exposure to the UV light source.

STATISTICAL CONSIDERATION AND DATA ANALYSIS

For sample size computation, a minimum of 85 subjects was required for this study, based on a level of significance of 5%, a development of erythema at 745mJ/cm^2 prevalence of 33.3% with a desired half-width of confidence interval of 10%, as noted from the reference study by Pai GS, 2002.[5] To compensate for the respondents that may be lost to follow-up, an additional 10% was added. However, no subjects were lost to follow-up. The total number of subjects who completed the study is 86.

Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables, median and IQR for non-normally distributed continuous variables, and mean and SD for normally distributed continuous variables. Chi-square test of association was used to determine the association of MED value of the patients and their Fitzpatrick skin type, ancestry, daily duration of sun exposure and sex. Spearman rho correlation analysis was used to determine the association of MED value to patient's age, then a scatter plot was generated for visual presentation of its values. Missing variables were neither replaced nor estimated. STATA 13.[1] was used for data analysis.

RESULTS

A total of 87 subjects were recruited to participate in the study. All were examined for eligibility. However, one volunteer was excluded as she had an underlying malignancy and was undergoing chemotherapy. The remaining 86 subjects were included and were able to complete the entire study duration and analysis.

DEMOGRAPHIC PROFILE OF THE STUDY PARTICIPANTS

The demographic profile of the study participants (Table 2) showed that majority were female (65.12%), and with a mean age of 31.98 + 8.15. Out of the 86 study participants, majority (82.56%) had no comorbidities. All were employed, with most working as service personnel (46.52%), health care professionals (34.88%), and security personnel (12.79%).

Most of the participants were pure Filipino (86.05%), with a smaller percentage having mixed ancestry as follows: East Asian (9.30%), Mediterranean (4.65%), and North European (1.16%). One participant ticked both East Asian, and Mediterra-

Table 4. Association of MED values to Sex, Fitzpatrick skin type, Ancestry and Sun exposure.

Characteristics	n	MED Values (mj/cm²)					p-value
		400	600	800	1,000	1,200	
Sex, frequency (%)							0.245
Male	30	3 (10)	6 (20)	11(36.67)	6 (20)	4 (13.33)	
Female	56	3 (5.36)	17 (30.36)	27 (48.21)	7 (12.5)	2 (3.57)	
Fitzpatrick skin type, frequency (%)							<0.001*
Type II	1	1 (100)	0	0	0	0	
Type III	20	2(10)	11 (55)	5 (25)	1 (5)	1 (5)	
Type IV	57	3(5.36)	12 (21.05)	31 (54.39)	9 (15.79)	2 (3.51)	
Type V	8	0	0	2 (25)	3 (37.5)	3 (37.5)	
Ancestry, frequency (%)							0.031*
Pure Filipino	74	3 (4.05)	17 (22.97)	35 (47.30)	13 (17.57)	6 (8.11)	
East Asian	7	2 (28.57)	3 (42.86)	2 (28.57)	0	0	
Mediterranean	4	0	3 (75)	1(25)	0	0	
North European	1	1 (100)	0	0	0	0	
Daily duration of sun exposure, frequency (%)							0.237
Minimal	53	6 (11.32)	15 (28.30)	24 (45.28)	5 (9.43)	3 (5.66)	
Moderate	31	0	8 (25.81)	13 (41.94)	7 (22.58)	3 (9.68)	
Severe	2	0	0	1 (50)	1 (50)	0	

nean as part of her mixed ancestry and was counted for both categories. Majority have Fitzpatrick skin types IV (66.28%) followed by type III (23.26%). For the daily duration of sun exposure, most (61.63%) had only minimal exposure, defined as less than 10 minutes of cumulative duration of daily sun exposure.

PRIMARY AND SECONDARY OUTCOME MEASURES

Most of the participants (44.19%) had an MED of 800mJ/cm^2, followed by a smaller percentage (26.74%) who had an MED of 600mJ/cm^2 (Table 3). For the subjective assessment to the MED testing, four participants experienced pruritus (with a score of 2-3/10 using a visual analog scale (VAS), and two reported pain or tenderness (score of 2/10 on VAS) on the MED testing sites. The same two study participants reported an adverse effect of burning sensation with a grade of 1 on the MED testing areas, defined as awareness of symptoms but easily tolerated.

ASSOCIATION OF MED VALUE TO AGE, SEX, FITZPATRICK SKIN TYPE, ANCESTRY AND SUN EXPOSURE

There is a significant association between study participants' MED for NB-UVB with respect to their Fitzpatrick skin type (p=<0.001) as more than half of participants with skin type IV (54.39%) had MED of 800 mJ/cm^2, and more than half of participants with skin type III (55%) had MED of 600mJ/cm^2 (Table 4). There is also a significant association between MED values and ancestry (p=0.031) as nearly half of pure Filipino participants (47.30%) had MED of 800mJ/cm^2. In contrast, there was no significant association between MED values and age (p=0.291), sex (p=0.245), and daily sun exposure (p=0.237).

DISCUSSION

A common method for determining the initial NBUVB dose is to estimate it based on the patient's Fitzpatrick SPT.[7,8] This method is frequently used in clinical practice as it is more convenient, but our basis for this method which is patterned after Caucasian skin, may result to suboptimal initial treatment delivery, especially for Filipinos who have a diverse racial ancestry (predominantly SPT III and IV), and are more pigmented than Caucasian skin.

The results of this study showed that Filipino adult patients seen in a tertiary hospital, wherein majority are pure Filipinos, and some with mixed ancestry of East Asian, Mediterranean and North European have a median MED value of 800 mJ/cm^2, IQR (600-800 mJ/cm^2). Based on this MED value, the initial dosage of NBUVB at 50-70% of the MED would translate to an initial dose of 400-560 mJ/cm^2. This finding can serve as a basis for a higher initial dosage compared to the more conservative method the tertiary hospital is currently using. It also supports the most recent guidelines for NBUVB phototherapy for psoriatic patients that recommends an initial dosage of 500mJ/cm^2 for patients with SPT III and IV[9], and the study of Lee et al. that recommended a higher starting dose in Asian patients with vitiligo who are also predominantly SPT III and IV.[10]

The study also noted a significant association between the patient's MED values and their variables which are ancestry,

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and examiner-assigned SPT. Majority of the pure Filipino participants had an MED range of 600-800mJ/cm^2; while those with East Asian ancestry had a range of 400-800mJ/cm^2. This suggests that determining the patient's ancestry and their SPT during their initial visit can also be a good basis on determining the patient's initial NBUVB dosage, as it has always been done using the latter variable.

The participants who joined the study also had only very minimal reports of pruritus, pain and burning sensation to the MED testing suggesting that in an ideal setting, determining the patient's MED should always be considered.

The limitation of this study is that it was conducted in a selected population in a tertiary hospital, which makes the results not representative of the entire Filipino population. Also, given the range of MED values on pure Filipinos, a standardized initial dose cannot be obtained. But considering the lack of study on MED values using NBUVB on Filipino skin, the results are still worthy of recognition in its attempt to serve as a guide for clinicians in determining the initial dosage of NB-UVB for their patients.

CONCLUSION

Majority of the participants have a median MED value of 800 mJ/cm2. Based on this MED value, the initial dosage of NBUVB at 50-70% of the MED would translate to an initial dose of 400-560 mJ/cm2. As there is no current definite guideline for the starting dose of NBUVB for Filipino skin, we can consider a higher starting dose for Filipino patients compared to the conservative approach most clinicians use. This can lead to a faster onset of efficacy, improvement, and eventually decreased number of treatment sessions that translates to less expense, improved quality of life, and patient satisfaction. Having said this, the authors of the study recommend future studies to determine if a higher initial NBUVB dosage can lead to faster clearance of skin lesions in Filipino patients with photo-responsive dermatoses.

REFERENCES

1. Cafardi J, Pollack B, Elmets C. Phototherapy. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K. Fitzpatrick's Dermatology in General Medicine. 8th ed. New York, NY: McGraw-Hill Companies Inc; 2012: p. 2841-2850.
2. Heckman CJ, Chandler R, Kloss JD, Benson A, Rooney D, Munshi T, et al. Minimal erythema dose (MED) testing. J Vis Exp 2013; 75: 50175. DOI: 10.3791/50175
3. Verallo-Rowell VM., Meneses M., Nunez J., Laureta R. Phototyping and multi-heritage skin of Asian-Filipinos in the Philippines. Skin in the Tropics: Sunscreens and Hyperpigmentations. Anvil Publishing Inc. 2001 pp.143-155
4. Reddy K, Lenzy M, Brown K, Gilchrest B. Racial considerations: Skin of color. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K. Fitzpatrick's Dermatology in General Medicine. 8th ed. New York, NY: McGraw-Hill Companies Inc; 2012: p. 91-103.
5. Pai GS. MED estimation for narrow band UV-B on type IV and type V skin in India. Indian J Dermatol Venereol Leprol 2001;67: 251-2. PMID: 17664763.
6. HOUVA4® User Manual, National Biologics Corporation, Ohio. 2012.
7. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. Arch Dermatol 1988; 124: 869-71. DOI: 10.1001/archderm.124.6.869.
8. Zanolli M, Feldman SR. Phototherapy Treatment Protocols. 3rd ed. Boca Raton, FL: Taylor & Francis; 2016.
9. Elmets CA, Lim HW, Stoff B, Connor C, Cordoro KM, Lebwohl M, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with phototherapy. J Am Acad Dermatol. 2019 Sep;81(3):775-804. doi: 10.1016/j.jaad.2019.04.042. Epub 2019 Jul 25. Erratum in: J Am Acad Dermatol. 2020 Mar;82(3):780. PMID: 31351884.
10. Lee H, Chu H, Oh SH. Investigation of suitable starting doses of narrowband UVB in Asian vitiligo patients: a pilot study. J Eur Acad Dermatol Venereol. 2017 May;31(5):894-897. doi: 10.1111/jdv.13933. Epub 2016 Sep 12. PMID: 27549434.