Journal of Pakistan Association of Dermatologists. 2020; **30(3)**: 428-433.

Original Article

Narrow-Band ultraviolet B phototherapy for the treatment of Iraqi patients with uremic pruritus

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Abstract

Objective We aimed to assess the efficacy and safety of NB-UVB phototherapy in relieving uremic pruritus.

Patients and Methods Over a period of 12 months, we recruited 17 patients with uremic pruritus having skin phototype III and more, aged from 21 to 67 years, 19(52.9%) females and 8(47.1%) male. They received NB-UVB, 2 sessions per week for 10 weeks. The response was assessed using 5-D itch scale.

Results There was a 60.7±29.2% reduction of 5D-itch score compared to baseline (19.53±3 versus 7.59±5.8, p<0.001). The mean cumulative dose of NB-UVB for one patient was 24.99 joule/ cm^2 (1.25 ± 0.6 j/ cm^2 per session). At the end of the trial, according to 5-D itch score criteria, 82.4% of patients were considered as a responder (good in 47.1%, very good in 35.3%) and after the treatment at follow up for 8 weeks, 35.7% developed pruritus again. Transient erythema was observed in 2 patients (10.5%) on phototherapy.

Conclusion In our population, with Fitzpatrick s skin phototypes 3-5, NB-UVB phototherapy seems to be safe and effective choice for uremic pruritus, albeit tentative in some patients. High doses were required to achieve a satisfactory response.

Key words
Phototherapy uremic pruritus.

Introduction

Pruritus in chronic kidney disease (CKD) is one of the most common and bothersome symptom with approximately 40-90% of patients on long-term maintenance dialysis experience this problem.[1] Pruritus can cause serious discomfort, anxiety, depression and sleeping disturbance, considerable skin damage and had substantial effect on quality of life.[2] To date, the mechanism of uremic pruritus remain poorly understood and therapeutic options are limited and unsatisfactory.[3] Understanding the pathophysiological mechanism was not yet achieved completely so no definite curative management was obtained.[4] The first line of management of uremic pruritus is a combination of emollients with systemic treatment like oral antihistamines, gabapentin, doxepin, naloxone, naltrexone, but unfortunately, the best treatment option for renal pruritus is still uncertain.[5,6]

Over the last 40 years, ultraviolet phototherapy was used for treatment of uremic pruritus all over the world especially for those patients who did not respond to medical therapy. In 1977, Gilchrest *et al.* were firstly treated a small groups of patients with uremic pruritus with ultraviolet B light (UVB) in a controlled clinical

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trial, they noticed generalized improvement of pruritus in some patients.[7,8] Tan *et al.* in 1991 conducted a meta-analysis study and concluded that for uremic pruritus, UVB phototherapy was the only successful treatment that showed a clinical significance.[9]

Different ultraviolet light has been used including, UVA, BB-UVB and NB-UVB. The definitive mechanism of NB-UVB in alleviating pruritus is not well established, however, the mechanism involves a mixture of effects in cell cycle kinetics, alterations in cytokine expression, effect on mast cells and immunomodulation.[10] NB-UVB also have a direct effect on divalent ions[11], suppresses histamine release from cutaneous mast cells[12] and alteration of cutaneous nerves.[13] The current published studies on the use of NB-UVB phototherapy for uremic pruritus are limited and on reviewing PubMed database using the key words uremic pruritus NB-UVB phototherapy, five English articles were detected with a total of 101 patients receiving this modality of treatment.[14-18] Evenmore, the efficacy and safety of NB-UVB treatment in patients with uremic pruritus with skin phototypes 3-5 has not been studied. In this study, we assess NB-UVB phototherapy in relieving uremic pruritus in *cohort* of patients with Fitzpatrick ´s skin phototypes 3-5.

Patients and Methods

A prospective, non-randomized clinical study was conducted at the Department of Dermatology and Venereology, Basra Teaching Hospital, Basra, Iraq, during the period from November 2016 to November 2017. Seventeen patients with CKD associated generalized pruritus were included. Their ages were ranged from 21 to 67 years and with Fitzpatrick III-V skin phototype. Inclusion criteria were being aged 18 years or older and unresponsiveness to the conventional treatment (emollients and antihistamine for 6 weeks). Patients with other dermatological causes of pruritus, systemic diseases which can cause pruritus, having parathyroid hormone >520 pg/ mL or serum calcium > 10.2 mg/ dl, pregnant or lactating women and history of cutaneous photosensitivity, eye cataract or skin cancer were excluded. A detailed history was taken from each patient regarding the onset and duration of pruritus, periodicity (constant, paroxysmal), severity, ameliorating and exacerbating factors, and response to previous therapy. Full physical and dermatological examination including assessment of Fitzpatrick's skin phenotype were done. Detailed explanation about the nature, course, duration and possible complications of the treatment was given and all participants signed a written informed consent. Patients were received NB-UVB phototherapy twice per week in nonconsecutive days for a total of 20 sessions (10 weeks) and maintained on their prior antipruritic treatment. The genital area was protected in all cases; eyes were also protected with UVB-blocking goggles. Patients were advised to use topical emollient following UVB exposure. The NB-UVB treatments were administered in a special cabinet (Waldmann 7001K, Waldmann Mediziniche Technik, Villingen Schwenningen, Germany) equipped with 20 100-W fluorescent lamps (TL01, Philips Co, Eindhoven, The Netherlands). Initial dose was 0.3 joule/ cm^2 and further doses were introduced according to the erythema response occurred at the previous session; if there was no erythema, a 0.1j /cm^2 increment was used for the next doses. If erythema was mild, a 0.1j /cm^2 increment every other treatment, while if persistent asymptomatic erythema, no further increase in the dose, If erythema with pain and blistering developed, sessions were stopped until symptoms faded out and then the dose was reintroduced with a 50% reduction of the last dose.[19]

Table 1 Demographic characteristics of patients with uremic pruritus treated with narrow-band UV-B

Characteristic	*Value*
Age range	21–69 years (mean ± SD*: 53.1 ± 11.6 years)
Gender	Male: 8 (47.1%), Female: 9 (52.9%)
Duration of pruritus	6–35 months (median = 18 months)
Skin phototype	Type III: 5 (26.3%), Type IV: 8 (52.6%), Type V: 4 (21%)
C D† of NB-UVB	24.99 J/cm^2
Mean dose/session ± SD	1.25 ± 0.6 J/cm^2
Dialysis (14 patients)	Male: 7 (46%), Female: 8 (54%)
Non-dialysis (3 patients)	Male: 1 (50%), Female: 1(50%)

*Standard deviation, †cumulative dose of NB-UVB

Table 2 5-D itch score in patients with uremic pruritus at baseline and during the trial, with percentage of score reduction as compared to first visit

Visits	*5-D itch score (mean ± SD*)*	*% of score reduction (mean ± SD)*	*P-value*
Baseline	19.53 ± 3.0	-	-
10th week	10.71 ± 3.9	45 ± 19.9%	<0.001
20th week	7.59 ± 5.8	60.7 ± 29.2%	<0.001

*Standard deviation

The severity of pruritus were assessed using the 5D itch scale. This scale was validated in many studies as an accurate and reliable method to assess the multidimensional nature of pruritus and it has ability to detect changes in intensity of pruritus over time.[20] The scale consist of five domains (5D): degree, duration. direction, disability and distribution of pruritus. The duration, degree and direction domains each included one item, while the disability domain had four items. All items of the first four domains were measured on a five-point Likert scale, while the distribution domain included 16 potential locations of itch, including 15 body part items and one point of contact with clothing or bandages. The scores of each of the five domains were achieved separately and then summed together to obtain a total 5-D score. The scores can potentially range between 5 (no pruritus) and 25 (most severe pruritus).

The pruritus intensity was measured at baseline, at 5 weeks, at end of treatment (10 weeks) and 8 weeks in the follow up period. The patient was considered poor responder if the reduction in the 5 D score was <25%, mild: 25%-<50% reduction, good: 50%-<75%, and very good: >75% reduction. According to the 5D-itch criteria, a reduction less than 50 % was considered as non-responder. Fifty percent or more or if the minimum score of 5 is recorded (corresponding to no pruritus) the patient was regarded as responder.[21]

Side effects were assessed and recorded at each visit, including: erythema, burning of skin, hyper pigmentation and blistering.

Statistical analysis was done by using SPSS (statistical package for social sciences) version 20. P value ≤0.05 was considered as the level of significance

Results

Seventeen patients were included in the study, 2 patients (11%) did not complete the course of treatment (one died and the other was submitted to surgery). Patients demographic characteristics were shown in **Table 1**.

The mean of the 5-D itch score at baseline and throughout the study periods were shown in **Table 2**.

Table 3 Grading the percentage reduction in the 5-D itch score at the end of the trial

Response	*% of 5-D itch score reduction*	*No. of patients (%)*
Poor	<25%	3 (17.6%)
Mild	25%–<50%	0 (0%)
Good	50%–<75%	9 (47.3%)*
Very good	>75%	7 (36.8%)*
Total		19 (100%)

*Regarded as responders (84.1% collectively)

Compared to the baseline, there was a 45±19.9% and 60.7±29.2% reduction of 5D- itch score mean at the end of the 5th and 10th week respectively ($p<0.001$). The percentage of reduction was 3% at the 1st week and consistently escalate up to 61% in the 10th week with no statistically significance between hemodialysis and non-hemodialysis patients.

At the end of the trial, scoring the response to treatment is shown in **Table 3**.

According to 5-D itch score criteria, the majority of patients (82.4%) were regarded as a responders. The cumulative dose of NB-UVB per patient was ranged between 18.25 j/cm^2 and 32.5 j/cm^2 and the mean cumulative dose was 24.99±7.5 j/cm^2 (mean per session=1.25±0.6 j/cm2). During 8 weeks follow up period, 9 patients (64.3%) had no recurrence of their symptoms, while 5 patients (35.7%) developed pruritus again (3 of them with the same baseline score and 1 patient above).

Discussion

In the present study we demonstrated that NB-UVB is an effective option in alleviating CKD associated pruritus. Using 5D-itch score most of our patients had moderate to severe pruritus (5D-itch score ranging from 14 to 24) with history of unresponsiveness to conventional medical treatments. The significant improvement in 5D-itch score (45% reduction) was observed after 10 sessions and continued to mount gradually over the subsequent treatments. Eventually, at the end of the trial, 82% of patients were regarded as a responder, with 61% reduction of the 5D itch score compared to baseline.

The effectiveness of NB-UVB in the treatment of uremic pruritus has been evaluated in many studies. For instance, Ada *et al.*[14] uses NB UVB to treat 20 Turkish patients with uremic pruritus (90% with Fitzpatrick phototype 3 and more). After 6 weeks period of treatment, 3 sessions each week, they noticed a significant improvement of the VAS (Visual Analog Scale) and pruritus scaling system compared to the baseline in 80% of cases, however, 6 months later they noticed a recurrence of the symptoms in 57% of the patients. Seckin *et al.*[15] treated 17 patients with CKD pruritus with NB-UVB measuring the pruritus with the same scoring system, 10(67%) of them have Fitzpatrick phototype 3, they noticed a remarkable improvement of pruritus in 60% of cases after 8 weeks, with 66% relapse rate. More recently, in a case-controlled study conducted by Wang *et al.*,[16] significant improvement of pruritus intensity in NB-UVB treated group (68.4%) compared to the control was reported. Our results were comparable to these studies but instead, we use 5-D Itch Score System in assessing the severity of pruritus in patients with CKD which we think is more precise and more accurate as a multidimensional scale. We also found a low relapse rate of pruritus in our patients after treatment. It is possible that the reason for the decrease in the rate of recurrence of pruritus is due to the fact that the doses of NB-UVB given to our patients were much higher than that reported in previous studies [

Ada and Seckin studies,[14,15] 200mj/cm^2 compared to 1.25j/cm^2 in our study] and we think that such high doses were sufficient enough to produce a durable and sustained improvement.

For our patients, the total cumulative dose of NB-UVB was 24j/cm^2 (mean was 1.25±0.6 j/cm^2 per session) which was much lower than the safe cumulative dose reported by Jin *et al.*[22] when they reviewed a 445 patients with various inflammatory skin diseases including psoriasis, vitiligo, atopic dermatitis and other dermatoses treated by NB-UVB with mean cumulative dose of 45.2 J/cm^2, they noticed no significant increase in incidence of skin malignancy among these patients.

No major side effects were reported, except for one patient who experienced a transient erythema and increase in pruritus intensity after the first session, an effect which faded out few hours later supporting the evidence that NB-UVB phototherapy is well tolerated with excellent safety profile.[23-25]

Limitations The major limitation of this trial was the small number of recruited patients and our results were considered as preliminary and need to be confirmed on large scale of patients.

Conclusions

NB-UVB phototherapy seems to be safe and effective choice for uremic pruritus, and should be considered as an option when conventional medical treatment was unsuccessful . For those patients with Fitzpatrick s skin phototypes 3-5, an appropriate doses of NB-UVB were required to achieve noticeable and sustained improvement.

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