Narrow band UVB phototherapy for the treatment of refractory renal pruritus among patients on hemodialysis

Mohammad Abusailik, MD*; Abdullah Alhasanat, MD*; Khaled Hamadeneh, MD**; Alsharif Mohammad Fawwaz, MD*; Adam Almuhisen, MD*; Mohammed Nawaiseh, MD*.**

ABSTRACT

Objective: To assess the efficacy of narrowband ultraviolet B phototherapy for the treatment of refractory renal pruritus among patients on hemodialysis.

Methods: This prospective multi-centered cohort study included 106 adult patients with renal failure on maintenance hemodialysis. These patients who presented with severe renal pruritus unresponsive to previous therapies, were treated with narrowband ultraviolet B phototherapy three times a week for four months. The initial therapeutic ultraviolet B dose was dependent on the skin phototype. The dose was increased by 20% if erythema appeared or by 40% if it did not. Evaluation of pruritus was carried out monthly during treatment and three months following treatment cessation using the 12-Item pruritus severity scale (PSS).

Results: There was a significant improvement in the degree of pruritus in the first three months of phototherapy. However, the improvement at the fourth visit was not significant. Pruritus severity scale decreased from a mean of 19.1 ± 1.9 at the initiation of phototherapy to 9.2 ± 3.9 at the end of treatment ($P < .001$), but increased to 12.9 ± 4.0 three months after cessation of treatment. The overall response rate was 78%. Although the relapse rate was 52%, the overall improvement from pretreatment state was significant ($p < .001$).

Conclusion: Since there was no significant improvement after the third visit and given that there was a high relapse rate after treatment discontinuation, we recommend starting an induction therapy (3 times a week) in the first three months, then continuing for maintenance therapy with the possibility of combining phototherapy with other systemic therapies. Narrowband ultraviolet B phototherapy is highly effective for the treatment of renal pruritus, but the clinical response is short-lived with a high relapse rate after discontinuation of phototherapy.

Key words: Phototherapy, Narrowband UVB, Renal pruritus, pruritus severity scale, chronic kidney disease-associated pruritus.

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INTRODUCTION

Renal pruritus (chronic kidney disease-associated pruritus) is a frequent and highly irritating and debilitating symptom of end stage kidney disease (1).

From the deparetments of:
* Department of Dermatology, Jordanian Royal Medical Services, Amman, Jordan.
** Department of Nephrology, Jordanian Royal Medical Services, Amman, Jordan.
*** Internship, Jordanian Royal Medical Services, Amman, Jordan.

Renal pruritus may be localized or generalized, paroxysmal or persistent (2), affecting 84% of patients with end-stage renal disease treated without dialysis (3). Renal pruritus may be generalized in up to 50% of patients (4). However, as a result of advancements in dialysis methods, the prevalence of renal pruritus has declined significantly (5). Hu et al. concluded that with effective and regular dialysis, pruritus could be alleviated in 40% of patients (2). Approximately, 41% of patients with end-stage renal disease on dialysis were found to be affected by pruritus (6). Meanwhile, in a recent meta-analysis that included 11,800 patients from different countries, it was found that the overall prevalence of renal pruritus among dialysis patients was 55% (7). There is a significant difference in the prevalence among different countries (6, 7). However, the occurrence of renal pruritus is not associated with gender, age, the duration of dialysis or the etiology of the renal failure (7, 8).

Pruritus tends to peak at night after two days without dialysis, is relatively high during treatment and is lowest during the day following dialysis (9, 10). Renal pruritus is an independent mortality predictor for patients on hemodialysis, with 15-21% higher mortality compared to those without pruritus (6, 11). Furthermore, pruritus negatively affects the patient's sleep and quality of life (4, 12, 13, 14, 15, 16).

The pathophysiology of renal pruritus is poorly understood (12, 17, 18). Proposed mechanisms include increased total number of mast cells in the skin and increased plasma histamine level in uremic patients (19, 20), high serum levels of parathyroid hormone (21, 22), calcium and phosphate (23), impaired stratum corneum hydration (9, 24), endogenous opioids (12, 25), and immunologic alteration characterized by a pro-inflammatory pattern (17, 26).

Treatment of renal pruritus is challenging, most of the available medications showed variable success. Topical therapies (e.g., emollients, topical steroids, topical calcineurin inhibitors, topical antipruritics such as calamine lotion and topical capsaicin) only marginally reduce localized pruritus. Topical therapies are not used for generalized pruritus because of cost limitations and risk of systemic absorption (12). Therefore, systemic therapy becomes essential. Available systemic therapies include oral antihistamine (27, 28), ondansetron, naltrexone (29, 30), nalfurafine (29, 31, 32), Difelikefalin (33**),** thalidomide (34), gabapentin (28, 35, 36), mast cell stabilizer, dupilumab (37), Mirtazapine (38), charcoal (39) and NB-UVB phototherapy (40). Unfortunately, the optimal therapeutic guidelines for renal pruritus remain both controversial and uncertain.

Phototherapy is safe and effective in the management of pruritus in all age groups (41, 42, 43) without many of the risks and adverse effects of systemic medications. This method involves the use of ultraviolet (UV) light in the management of various forms of dermatoses (40). Coven (43) found that NB-UVB was more effective than broadband (BB-UVB) in the treatment of psoriasis. Moreover, NB-UVB was found to be effective in both generalized (40) and refractory renal pruritus uncontrolled by conventional treatments (45).

NB-UVB is a form of phototherapy that uses artificial ultraviolet light in a wavelength between 311-313 nm to generate therapeutic effects via photochemical reactions. Its main mechanism of action is not entirely understood, but involves inhibition of DNA synthesis, effects on the function of Langerhans cells and lymphocytes, mast cell apoptosis, as well as alteration of cytokines production, and immunosuppressive activity (46, 47, 48).

Few studies have assessed chronic kidney disease-associated pruritus, and to the best of our knowledge, there are no studies evaluating the NB-UVB in the treatment of renal pruritus in Jordan. Therefore, the purpose of the study was to investigate the effectiveness, response and relapse rate of NB-UVB treatment of renal pruritus specifically among Jordanian Arabic

patients. We expect that this article will increase awareness of the physicians and other healthcare professionals about this modality of treatment, and it will provide a therapeutic guideline for the treatment of refractory renal pruritus with NB-UVB phototherapy.

METHODS

The current study is a prospective cohort multi-centered study that was approved by the Jordanian Royal Medical Services (JRMS) ethics committee. This study was conducted in the period between September 2018 and November 2019 and involved 106 patients with end-stage renal disease on maintenance hemodialysis in the hospitals of JRMS, all of whom met the selection criteria.

In order to be included in the study, the patients had to meet the following inclusion criteria:

1. Patients diagnosed with end-stage renal disease - associated pruritus on maintenance hemodialysis (Stage 5 D).
2. Age more than 18 years.
3. Previous treatment with at least two topical or systemic antipruritic therapy for at least 3 months without showing any clinical response.

Meanwhile, the following exclusion criteria were also applied:

1. Patients unwilling to participate in the study.
2. The presence of associated co-morbidities or dermatological conditions that lead to localized or generalized pruritus.
3. Contraindications to phototherapy such as photosensitive skin diseases (eg., lupus nephritis), or a previous history of cutaneous malignancy (eg., Basal cell carcinoma).
4. Pregnant or breastfeeding women.
5. Patients unwilling to complete follow up or patients who did not complete follow up.
6. Serum calcium level more than 10 mg/dl and hemoglobin level less than 10 g/dl, which ensured the exclusion of pruritus caused by hypercalcemia or iron deficiency anemia.

An informed consent had been taken from each patient, after which a detailed history and clinical examination were elicited for each case, with a particular emphasis on pruritus. The Fitzpatrick skin phototype was assessed to guide treatment with phototherapy.

Each patient had been asked to fill in a questionnaire of a 12-item pruritus severity scale (12-PSS), then the patient was subjected to the treatment with NB-UVB phototherapy three times a week for four months (51 sessions for each patient). Meanwhile, the patients were asked to continue with their previous therapy for pruritus. A 12-items pruritus severity scale was assessed on a monthly basis during the treatment and three months after cessation of the treatment. Any side effects of phototherapy, such as erythema, burning sensation, stinging, scaling and bullae formation were assessed following each phototherapy session.

The 12-PSS is a one-page instrument consisting of 12 items that assess different aspects of pruritus (49; appendix A). As the questionnaire was originally in English, concerns were raised regarding the reliability and validity of the responses, so an arabic translated version of the instrument was created (Appendix B). The items were grouped into five domains: duration of pruritus (one question: Q1), frequency and impact of pruritus on daily activities and mood (four questions: Q2 to Q5), scratching assessment as a response to pruritus (four questions: Q6 to Q8

and Q12), pruritus intensity (two questions: Q9 and Q10), and pruritus extent (one question: Q11). Total score can range from 3 (minimal pruritus) to 22 (most severe pruritus).

The initial therapeutic UVB dose was dependent on the skin phototype (Table I). There were no patients with Fitzpatrick skin type 1. After each phototherapy session, the dose was increased by 40% if no erythema appeared. Minimal erythema had developed in six patients only, which necessitated an increase in the UVB dose of only 20% instead of 40%.

Table I: Initial therapeutic UVB dose according to skin phototype.

Fitzpatrick skin phototype	Initial therapeutic dose
2	120 mj/cm2
3	150 mj/cm2
4	200 mj/cm2
5	300 mj/cm2
6	500 mj/cm2

The patients' therapeutic response was defined in terms of a >50% reduction in the 12-item PSS compared with the baseline score, while a relapse was defined as a >50% increase in the 12-item PSS three months after phototherapy discontinuation with the patients who had achieved a therapeutic response.

We were careful to ensure the phototherapy sessions were conducted on the same day of the hemodialysis sessions. Therefore, no additional visits to the hospital were required, which resulted in higher acceptance and compliance to the treatment plans among the patients.

Statistical analysis

SPSS version 25.0 was used in our analysis. After the data (scores) had been entered into a Microsoft Excel 2010 worksheet and configured properly, they were imported into SPSS. Mean (± standard deviation) have been used to describe continuous variables (i.e. age). Count (frequency) have been used to describe other nominal variables (i.e. gender). All statistical tests were two-sided and p values < .01 were considered statistically significant. All underlying assumptions were met, unless otherwise indicated.

We have performed two-way repeated measures ANOVA to study the difference in mean PSS scores among the visits and between males and females. Normality assumption was not met. However, this assumption is not required if the sample size is larger than 25 participants. Mauchly's test was done to study the sphericity assumption, while Greenhouse-Geisser correction was used since the sphericity assumption was not met.

As the normality assumption was not met, we have performed Kendall tau B test to assess if there is a correlation between the duration of dialysis and the response rate.

RESULTS

A total of 106 (56 females and 50 males) Jordanian patients with end stage renal disease on maintenance hemodialysis were included in this study and subjected to final analysis. The mean age of patients were 56 ±11 years, with the youngest being 18 and the oldest being 72 years of age. Twenty six (24.5 %) patients were younger than 50 years of age. Thirty six (33.9%) patients were in the age group between 51 to 60 years and 44 (41.5%) patients were older than 61 years. The causes of hemodialysis were diabetic nephropathy in 50 patients, hypertensive nephropathy in 38 patients and miscellaneous causes in the rest of patients. The mean duration of the hemodialysis was 5.8 ± 2.9 years. An additional three patients died before they completed their phototherapy sessions; therefore, they were dropped out of the study. There were no significant side effects that necessitated discontinuation of the treatment; six patients had developed mild erythema that was managed by reduction of phototherapy dose on subsequent sessions. While another six patients had developed exacerbation of pruritus that was tolerable and did not interfere with subsequent sessions. No other side-effects were noted.

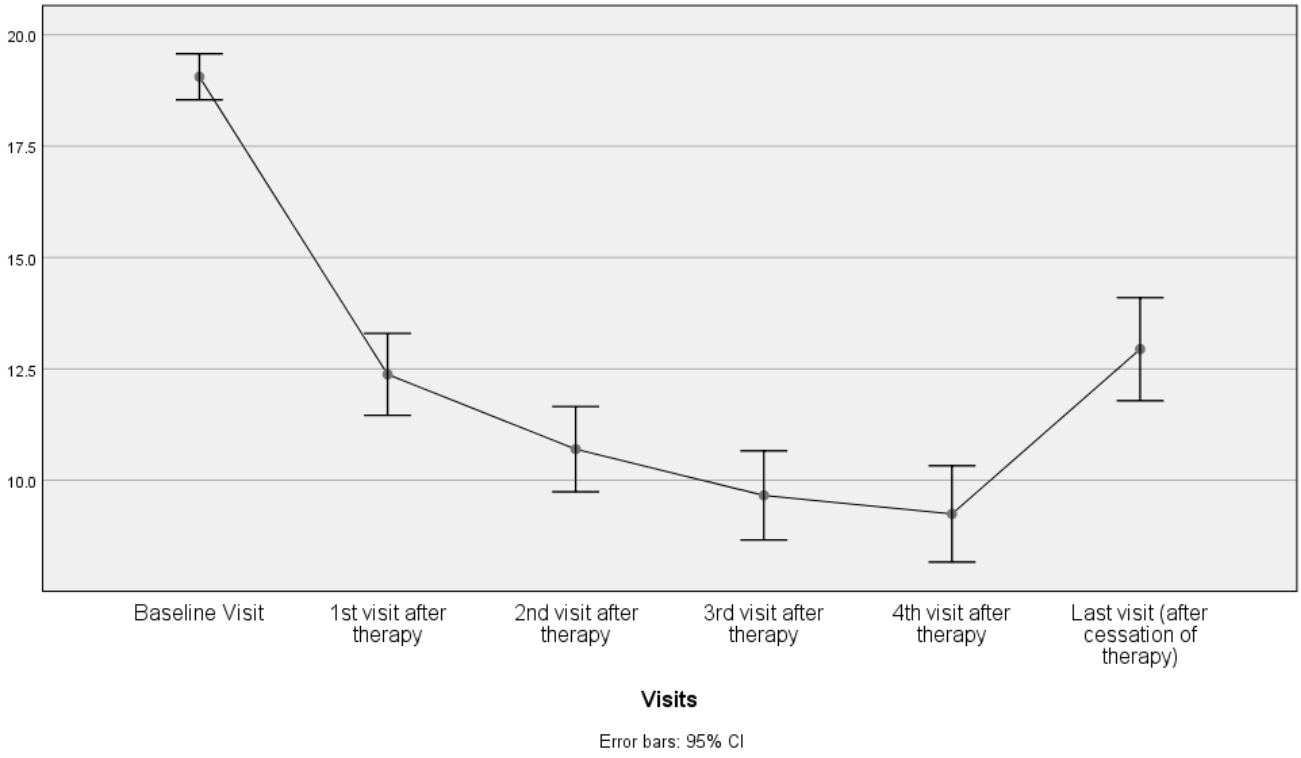
The mean of the 12-PSS before initiation of the treatment was 19.1 ± 1.9, then stepped down to 12.3 ± 3 by the end of the first month. The 12-PSS at the end of the second month was 10.7 ± 3.7, at the end of the third month was 9.7 ± 3.6 and at the end of the fourth month was 9.2 ± 3.9, but increased to 12.9 ± 4 three months after cessation of the treatment (Table II). The mean scores of all visits were significantly lower (p < .001) than the baseline visit mean score, with a mean difference of 6.8 for the first visit, 8.4 for the second visit, 9.4 for the third visit, 9.9 for the fourth visit and 6.2 for the last visit.

Table II: Mean ± SD of the 12 item pruritus severity scale (12-PSS) for each visit with the mean difference with each subsequent visit

Visit	Total and Gender	Baseline visit	First visit after UVB	Second visit after UVB	Third visit after UVB	Fourth visit after UVB	Last visit
Mean and SD	**Total**	19.1 ± 1.9	12.3 ± 3.0	10.7 ± 3.7	9.7 ± 3.6	9.2 ± 3.9	12.9 ± 4.0
	Male	18.6 ± 1.7	12.0 ± 3.1	10.6 ± 3.4	9.4 ± 3.5	9.0 ± 3.8	13.2 ± 4.1
	Female	19.5 ± 2.0	12.8 ± 3.5	10.8 ± 3.6	9.9 ± 3.8	9.5 ± 4.1	12.7 ± 4.4
Mean difference with subsequent visit*	**Total**	6.7 [5.7 to 7.6]	1.7 [1.3 to 1.9]	1.0 [0.7 to 1.3]	0.4 [0.16 to 0.7]	-3.7 [-4.6 to -2.7]	-
	Male	6.6 [5.3 to 7.9]	1.4 [0.9 to 1.8]	1.1 [0.7 to 1.5]	0.4 [-0.1 to 1.0]	-4.1 [-5.5 to -2.7]	-
	Female	6.7 [5.1 to 8.2]	1.9 [1.5 to 2.3]	1.0 [0.6 to 1.3]	0.4 [-0.2 to 1.0]	-3.3 [-4.5 to -1.9]	-
***P*-value**	**Total**	< .001	< .001	< .001	0.016	< .001	-
(after bonferroni correction)	**Male**	< .001	< .001	< .001	0.195	< .001	-
	Female	< .001	< .001	< .001	0.472	< .001	-

Mauchly's test indicated that the assumption of sphericity had been violated (χ^2 (14) = 543.8, p < .001), therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity (ε = 0.47). Repeated measures ANOVA showed that there was a statistically significant improvement in pruritus measured using 12-PSS score, F (2.3, 247.7) = 320.2, p < .001, ηp 2 = 0.75 (Fig. 1). Moreover, we found no significant difference between males and females in the 12-PSS score of each visit, F (1,104) = 0.492, p = .484, ηp 2 = 0.004.

Figure 1: Estimated means of the 12-PSS score before, during and after UVB phototherapy**.**



Post hoc analysis using Bonferroni correction indicated that the mean 12-PSS score was lower in each subsequent visit during the treatment duration (Table II).

The fourth treatment visit was the only exception; as the mean difference of improvement between the third and fourth visit in males was 0.4 (*P* value = .195) and in females was 0.4 (*P* value = .472), which was not statistically significant. Moreover, it showed that there was a significant increase in the mean 12-PSS after cessation of treatment (p < .001). Although there was some worsening of the symptoms after treatment discontinuation, the overall mean score was significantly lower than the baseline pre-treatment score (Mean difference = -6.1, p < .001).

We have computed Kendall tau B test to assess whether there was a correlation between the duration of the dialysis (M = 5.9 ± 3 years) and the response rate. Here, there was no statistically significant relationship between the two variables (r = .2, n = 106, p = .095).

The number of patients who achieved therapeutic response (reduction in the 12-items PSS of more than 50%) after the first month is 24, after the second month is 40, and after the third month is 16. The overall response rate was 76% (80 patients). Two patients showed complete response and achieved a minimum score of 3 points at discontinuation of the treatment. Twenty six patients failed to achieve therapeutic response, with six of these exhibiting an exacerbation of the pruritus and an increase in 12-PSS score as a side effect of the phototherapy. Meanwhile, the remaining 20 patients achieved a slight reduction in 12-PSS score, which was of value to some of these patients.

Of the 80 patients who experienced a therapeutic response, 42 (52%) relapsed 3 months after discontinuation of treatment with an increase in the 12-PSS of more than 50%. However, there is a reduction in the mean score from 19 before initiation of the treatment to 12.9 after 3 months of therapy discontinuation. This improvement was found to be beneficial to many of the patients and leads to improvement in quality of life, even though they are considered statistically relapsed patients.

DISCUSSION

In this study, we investigated the efficacy of NB-UVB as an add-on therapy to relieve renal pruritus and aid in improvement in quality of life for those patients with end-stage renal disease on maintenance hemodialysis.

We observed that there was a significant improvement in pruritus in the first 3 months of phototherapy. However, the degree of improvement in the fourth month was not significant. The overall response rate was 76% (80 patients) and the response rate in the first 2 months was 60% (64 patients). Of those who showed therapeutic response, 42 patients relapsed 3 months after the discontinuation of the treatment. Even though there was significant relapse after discontinuation of treatment, the overall improvement from pretreatment state was significant. There was no significant difference in treatment response and relapse rate between males and females. Furthermore, there was no correlation between the response rate and the duration of dialysis.

The majority of our patients reported improvement in their pruritus rapidly during the first month, with added benefits and significant reduction in the 12-PSS score for the following two months. No remarkable added benefits occurred in the fourth month of therapy. A response rate of 75% for such debilitating treatment resistant symptoms was considered by the patients to be a successful treatment in comparison with their previous therapies. However, high relapse rate (52%) three months after discontinuation of the treatment has alerted us to question about the importance of maintenance phototherapy (e.g. once weekly phototherapy session). Hence, we are considering starting an induction therapy (three times a week) in the first three months, then continuing for maintenance therapy (once a week). This issue requires further evaluation in future studies.

Phototherapy as a therapeutic modality for renal pruritus has been evaluated in many studies. Seckin et al. (40) found a response rate of 60% and a relapse rate of 66.7% after eight weeks of treatment with NB-UVB three times per week for end stage renal disease patients. When compared to our study, this lower response rate and higher relapse rate compared to those in our study may be due to the shorter duration of the phototherapy. EL-Kamel et al. (50) reported a response rate of 63% to NB-UVB alone and a response rate of 76% to combined treatment with NB-UVB and gabapentin. However, the relapse rate was much lower in the patients treated with

NB-UVB and gabapentin (12.5%) than those treated with NB-UVB alone (57%). In addition to the aforementioned maintenance phototherapy (e.g. once weekly phototherapy session), combining NB-UVB phototherapy with other systemic therapies could be the answer to reducing the high relapse rate in patients treated with NB-UVB alone. Further studies are needed to assess the effectiveness of combination therapy on decreasing relapse rate.

A study conducted on fifteen patients with ESRD on hemodialysis experienced significant improvement in pruritus intensity compared to a control group, those patients were treated three times per week for six weeks with NB-UVB phototherapy. The drawback of this study that there was no long-term follow up and it did not examine the risk of relapse after discontinuation of the treatment (51). Nugroho et al. found similar therapeutic effect of NB-UVB in reducing the intensity of renal pruritus, in addition to reducing the levels of serum ferritin, which plays an important role in the inflammation process in renal pruritus patients (52).

Not only patients with ESRD on hemodialysis, but also patients on peritoneal dialysis could benefit from phototherapy. Sapam et al. noted that NB-UVB phototherapy was helpful as an add-on therapy in relieving symptoms of uremic pruritus in patients on peritoneal dialysis (53). The response rate was 90.4% (19 out of 21 patients) and the relapse rate was 43% (6 out of 14 patients who have follow up data), which is comparable to the findings of our study. Moreover, substantial improvement in pruritus intensity was reported in patients with ESRD stage 4 and 5 not undergoing maintenance hemodialysis or peritoneal dialysis after NB-UVB phototherapy (54). Therefore, this modality of treatment could be used in any patient with ESRD who suffers from renal pruritus, regardless of the stage of ESRD.

In contrast to our study, Ko et al. (55) found that phototherapy had no significant effect in reducing pruritus intensity in refractory uremic pruritus. These negative results might be due to the small sample size (21 patients) and the short treatment period (six weeks).

Phototherapy is a safe modality for pruritus treatment, only six patients suffered from mild erythema, which was well tolerated by the patients and did not necessitate treatment discontinuation. This finding is accordant with previous studies, which showed that phototherapy was well tolerated with only few mild side effects (56, 57).

With this high response rate, the satisfaction by our patients, the improved quality of life, and the availability of NB-UVB phototherapy in most hospitals in Jordan, we recommend NB-UVB phototherapy for every patient with refractory renal pruritus that doesn't respond to conventional therapies. The disadvantages of phototherapy are the need for frequent visits to the hospital, phototherapy contraindications and high relapse rate that may necessitate maintenance phototherapy or a combination of NB-UVB and other systemic therapies.

Limitations and strengths

The findings of this study have to be seen in the light of some limitations. First, the lack of control group restricts our ability to establish a strong cause effect relationship. Second, the sample size was relatively small to detect a profound effect. However, our study included 106 patients from multiple hospitals, which is more than other studies that evaluated phototherapy for management of refractory renal pruritus. Patients were examined and treated by different doctors; this might contribute to lessen detection bias. Also, our study followed the patients for 7 months which is more than other studies. This is important to detect the effect, as there is a lag between UVB exposure and treatment effect (31).

Further randomized controlled studies with a larger sample size are needed to exclude the effect of other confounding factors and placebo effect. In addition, more studies are required to

evaluate other treatment schedules including maintenance therapy and phototherapy combined with other systemic therapies.

CONCLUSION

Appendix A: 12 items pruritus severity scale (12-PSS).

	Question	Possible answers	Scoring
(1)	How often did you feel pruritus within the last three days?	(i) All time	3 points
		(ii) All morning/ afternoon/ evening/ night. Long itch episodes.	2 points
		(iii) Occasionally, short itch episodes	1 point
(2)	Did pruritus hinder your ability to do simply things, like watching TV, hearing music, etc.?	(i) Yes	1 point
		(ii) No	0 points
(3)	Did you feel irritated or nervous because of your itching?	(i) Yes	1 point
		(ii) No	0 points
(4)	Did your pruritus cause you depressed?	(i) Yes	1 point
		(ii) No	0 points
(5)	Did your pruritus impede your work or learning abilities?	(i) Yes	1 point
		(ii) No	0 points
(6)	Did you scratch your skin because of itching?	(i) Yes	1 point
		(ii) No	0 points
(7)	Did scratching bring you relief?	(i) Yes	0 points
		(ii) No	1 point
(8)	Were you able to refrain from scratching?	(i) Yes	0 points
		(ii) No	1 point
(9)	Did you wake up during last night because of pruritus?	(i) No	0 points
		(ii) Yes, 1-2 times	1 point
		(iii) Yes, 3-4 times	2 points
		(iv) Yes, 5 and more times	3 points
(10)	Could you assess the severity of your pruritus within last 3 days?	(i) Very mild	1 point
		(ii) Mild	2 points
		(iii) Moderate	3 points
		(iv) Severe	4 points
		(v) Very severe	5 points
(11)	Could you indicate pruritus location?	(i) Single locations of pruritus	1 point
		(ii) Large body area	2 points
		(iii) Generalized pruritus	3 points
(12)	Are excoriations or other scratch lesions present?	(i) Yes	1 point
		(ii) No	0 points

NB-UVB phototherapy is an effective, beneficial, safe and available modality of treatment for patients with refractory renal pruritus, even if no complete response occurred. The drawback of this treatment remains the high relapse rate. Further studies are needed to determine the most suitable therapeutic regimes, the possible need for maintenance phototherapy, or combination therapy with other systemic agents and to determine which patients are more likely to benefit from phototherapy.

Appendix B: Arabic translation of the 12-PSS that was answered by our patients.

	السؤال	الإجابات المحتملة	النقاط
(1)	كم مرة شعرت بالحكة خلال الثلاثة أيام الماضية؟	(i) كل الوقت	3
		(ii) لفترة طويلة في الصباح أو في المساء أو في الليل	2
		(iii) لفترة قصيرة	1
(2)	هل تعيق الحكة قدرتك على القيام بأشياء بسيطة ، مثل مشاهدة التلفاز والاستماع إلى الموسيقى وما إلى ذلك؟	(i) نعم (ii) لا	1 0
(3)	هل شعرت بالغضب أو العصبيه بسبب الحكة؟	(i) نعم (ii) لا	1 0
(4)	هل تسبب لك الحكة الاكتئاب؟	(i) نعم (ii) لا	1 0
(5)	هل عرقلت الحكة عملك أو قدراتك في التعلم؟	(i) نعم (ii) لا	1 0
(6)	هل تقوم بخدش بشرتك بسبب الحكة؟	(i) نعم (ii) لا	1 0
(7)	هل خدش الجلد يجلب لك الراحة من شعور الحكة؟	(i) نعم (ii) لا	0 1
(8)	هل مررت بأوقات (ساعة / يوم / أكثر) كنت قادرًا فيها على الامتناع عن خدش جلدك؟	(i) نعم (ii) لا	0 1
(9)	هل استيقظت خلال الليلة الماضية بسبب الحكة؟	(i) لا (ii) مرة أو مرتين (iii) ثلاثة او اربع مرات (iv) خمس مرات أو أكثر	0 1 2 3
(10)	كيف تقيم شدة الحكة في غضون الثلاثة أيام الماضية؟	(i) خفيفة جدا (ii) خفيفة (iii) متوسطة (iv) شديدة (v) شديدة جدا	1 2 3 4 5
(11)	هل يمكنك تحديد موقع الحكة؟	(i) منطقة واحدة من الجسم (ii) عدة مناطق من الجسم (iii) كل الجسم	1 2 3
(12)	هل توجد آثار الخدوش على جسمك ؟	(i) نعم (ii) لا	1 0

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