

Efficacy of Narrow Band Ultraviolet B on Renal Pruritus in Patients with Chronic Kidney Disease

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Abstract

Background: Pruritus is a frequent and troublesome symptom in patients with chronic renal failure receiving hemodialysis. However, it also may occur in patients on conservative uremia treatment or undergoing continuous ambulatory peritoneal dialysis. Narrowband ultraviolet B phototherapy may be an effective treatment for patients with uremic pruritus.

Aim of Study: The current study was conducted to examine the effect of narrow band ultraviolet B on renal pruritus in patients with chronic kidney disease.

Subjects and Methods: Thirty patients with renal pruritus participated in this study. Their ages ranged from 40-60 years. They were selected from Hemodialysis Unit of Mansura University Hospitals and were divided randomly into two equal groups. Group (A) composed of 15 patients who received narrow band ultraviolet B 3 times/week for 6 weeks and medical treatment (oral antihistaminic and topical emollients). Group (B) composed of 15 patients who received only their medical treatment (antihistaminic and topical emollients). Method of evaluation was measurements of VAS and 5-D itch scale.

Results: There was a significant decrease in severity of pruritus in ultraviolet group when compared with the control group.

Conclusion: Narrow band ultraviolet B can be considered as an effective method in decreasing severity of pruritus in patients with chronic kidney disease.

Key Words: *Chronic kidney disease – Narrow band ultraviolet B – Renal pruritus.*

Introduction

PRURITUS is an intense symptom. People with pruritus often have difficulties resisting the urge to scratch itchy areas. Uremic pruritus is a disabling

symptom affecting approximately 50% of patients undergoing maintenance hemodialysis [1].

The pathogenesis of pruritus in chronic kidney disease patients receiving hemodialysis is multifactorial. Different theories as to the cause of pruritus include metabolic disequilibrium, endocrine disorders, inadequate dialysate, peripheral nervous system neuropathies, immune system derangement, opioidergic system involvement, and histamine and serotonin involvement [2].

The clinical features of renal pruritus are variable. The pruritus may be constant or intermittent. The back is the most commonly affected area, but arms, head, and abdomen are also commonly affected. Excoriations with no primary lesions, and sparing of the butterfly area of the back are typical. Patients with end stage renal disease, especially if due to diabetes mellitus, frequently develop keratotic nodules that on biopsy show a perforating disorder. These represent prurigo nodules and are a sign for severe and long-term pruritus [3].

Severe pruritus not only negatively affects quality of life, including sleep quality, daily functioning and emotional well-being, but it is also associated with poor disease prognosis in chronic kidney disease patients [4].

Topical products, such as moisturizers or emollients, and oral antihistamines are used for easing itchiness, but their effects are temporary and marginal [5].

Ultraviolet based therapy (phototherapy and photochemotherapy) can decrease severity of renal pruritus patients without many of the risks and side effects of systemic medications [6].

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The therapeutic effect on renal pruritus has been attributed to UVB-produced dermal mast cell apoptosis and decreases in pruritogenic cytokine (e.g. IL-2) production [7].

Subjects and Methods

Thirty patients who had renal pruritus participated in this study. Their ages ranged from 40 to 60 years. The participants were selected from Hemodialysis Unit of El-Mansura University Hospitals. The study conducted four months from May 2018 to August 2018. The patients were randomly assigned into two equal groups (15 patients for each group):

Group A (Study group): This group includes 15 patients with renal pruritus who received ultraviolet phototherapy (Narrowband Ultraviolet B) and medical treatment (oral antihistamines and topical emollients).

The treatment was conducted for 6 weeks (3 times/week).

Group B (Control group): This group includes 15 patients with renal pruritus received only medical treatment (oral antihistamines and topical emollients).

The potential participants were excluded if they had pruritus that could be explained by other systemic, dermatological or psychological causes, if they had change in consciousness and if they had febrile condition, if they had allergy to phototherapy and sunlight, if they had skin cancer.

Equipment used:

1- Measurement tools:

- Visual analogue scale (VAS):

A visual analogue scale consisting of a 10-cm horizontal line. The origin of the line on the left side is designated "no itch" and the end of the line on the right side is designated "worst itching ever" [8].

- The 5-D itch scale:

The 5-D itch questionnaire was specifically developed to be a measure of itch that is brief (one page), easy and multidimensional. The five domains are degree, duration, direction, disability and distribution [9].

2- Therapeutic equipment:

- Narrow band ultraviolet B (NB-UNB) Unit:

Waldmann (UV7002) lighting is equipped with 211 amps F79/120 W-TL01, which have a radiation spectrum of 311-nm to 313nm with a maximum at 311nm used for UVB-311 therapy.

Procedures of the study:

1- Measurement procedures:

Visual analogue scale (VAS):

Severity of pruritus was assessed by asking the patients to make a mark on the scale that corresponds to the relative severity of itch currently being experienced. This mark is made with a pen or pencil on the line that is 10-cm long. The score of visual analogue score (VAS) is the number of centimeters to the nearest millimeter between the origin of the scale on the left side and the mark on the scale made by the patient [8].

- The 5-D itch scale:

Severity of pruritus was assessed by 5-D itch scale as follow:

The scores of each of the five domains are achieved separately and then summed together to obtain a total 5-D score. 5-D scores can potentially range between 5 (no pruritus) and 25 (most severe pruritus). The three domains (duration, degree and direction) are equal to the value indicated below the response choice (range 1-5). The disability domain includes four items that assess the impact of itching on daily activities: Sleep, leisure/social activities, house work/errands and work/school. The score for the disability domain is achieved by taking the highest score on any of the four items. For the distribution domain, the number of affected body parts is tallied (potential sum 0-16) and the sum is sorted into five scoring bins: Sum of 0-2= Score of 1, sum of 3-5=Score of 2, sum of 6-10= Score of 3, sum of 11-13=Score of 4, and sum of 14-16=Score of 5 [9].

Measurements were taken before the treatment (pre-treatment) and after 6 weeks (post-treatment).

2- Treatment procedures:

The treatment protocol was presented under the following headings:

Narrow band ultraviolet B (NB-UVB) procedure:

During the 6 week intervention period, Narrow-band ultraviolet B was administered to the whole body surface 3 times a week using ultraviolet cabinet. Starting UVB dose was 150mJ/cm² for skin types I-II, 200mJ/cm² for skin types III-IV. Dosages were increased in each treatment session by 20% if there was no erythema. In case of mild to moderate erythema, the dose was maintained. If severe erythema and/or bulla formation occurred, treatment was paused until the reaction subsided and the subsequent doses were increased by 10%. Patients were also evaluated for adverse events

such as erythema, xerosis and exacerbation of pruritus associated with phototherapy in each visit. All patients were placed in comfortable position and asked to wear protective goggles before entering the machine [10].

Statistical procedures:

Descriptive statistics and *t*-test were conducted for comparison of the mean age of both groups. Unpaired *t*-test was conducted for comparison of VAS and 5-D itch scale between both groups. Paired *t*-test was conducted for comparison between pre and post treatment mean values of VAS and 5-D itch scale in each group. The level of significance for all statistical tests was set at $p < 0.05$. All statistical tests were performed through the statistical package for social sciences (SPSS) version 19 for windows (IBM SPSS, Chicago, IL, USA) [11].

Results

1- *Results of statistical analysis of visual analogue scale (VAS):*

- *Pre and post treatment mean values of VAS of group A:*

The mean \pm SD VAS pre treatment of group A was 7.93 ± 1.03 and that post treatment was 5.6 ± 0.73 . The mean difference between pre and post treatment was 2.33 and the percent of change was 29.38%. There was a significant decrease in the VAS of group A post treatment compared with that pre treatment ($p=0.0001$) (Table 1, Fig. 1).

Table (1): Paired *t*-test for comparison between pre and post treatment mean values of VAS of group A.

	VAS X \pm SD	MD	% of change	<i>t</i> - value	<i>p</i> - value	Sig.
Pre treatment	7.93 \pm 1.03	2.33	29.38	8.63	0.0001	S
Post treatment	5.6 \pm 0.73					

X : Mean.
p-value: Probability value.
t-value: Paired *t*-value.

MD : Mean difference.
SD \pm : Standard deviation.
S : Significant.

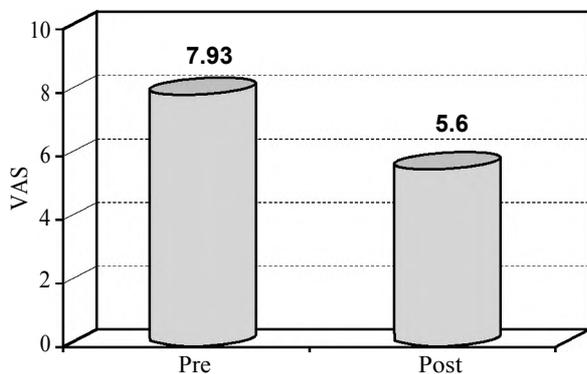


Fig. (1): Pre and post treatment mean values of VAS of group A.

- *Pre and post treatment mean values of VAS of group B:*

The mean \pm SD VAS pre treatment of group B was 7.46 ± 1.4 and that post treatment was 6.73 ± 1.57 . The mean difference between pre and post treatment was 0.73 and the percent of change was 9.78%. There was a significant decrease in the VAS of group B post treatment compared with that pre treatment ($p=0.0001$) (Table 2, Fig. 2).

Table (2): Paired *t*-test for comparison between pre and post treatment mean values of VAS of group B.

	VAS X \pm SD	MD	% of change	<i>t</i> - value	<i>p</i> - value	Sig.
Pre treatment	7.46 \pm 1.4	0.73	9.78	6.2	0.0001	S
Post treatment	6.73 \pm 1.57					

X : Mean.
p-value: Probability value.
t-value: Paired *t*-value.

MD : Mean difference.
SD \pm : Standard deviation.
S : Significant.

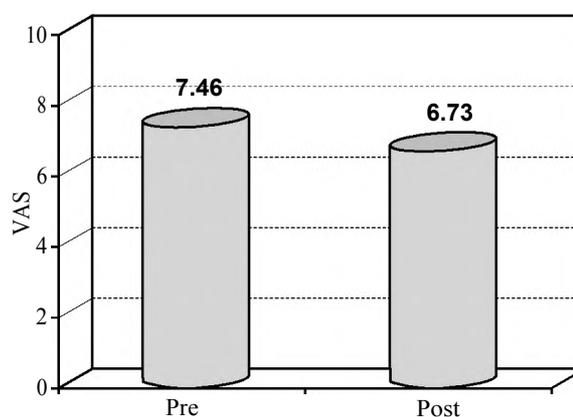


Fig. (2): Pre and post treatment mean values of VAS of group B.

- *Pre treatment mean values of VAS of both groups (A and B):*

The mean \pm SD VAS pretreatment of the group A was 7.93 ± 1.03 and that of the group B was 7.46 ± 1.4 . The mean difference between both groups was 0.47. There was no significant difference in the VAS between both groups pre treatment ($p=0.3$) (Table 3, Fig. 3).

Table (3): *t*-test for comparison between pre treatment mean values of VAS of both groups (A and B).

	VAS X \pm SD	MD	<i>t</i> - value	<i>p</i> - value	Sig.
Group A	7.93 \pm 1.03	0.47	1.03	0.3	NS
Group B	7.46 \pm 1.4				

X : Mean.
p-value: Probability value.
t-value: Unpaired *t*-value.

MD : Mean difference.
SD \pm : Standard deviation.
NS : Non significant.

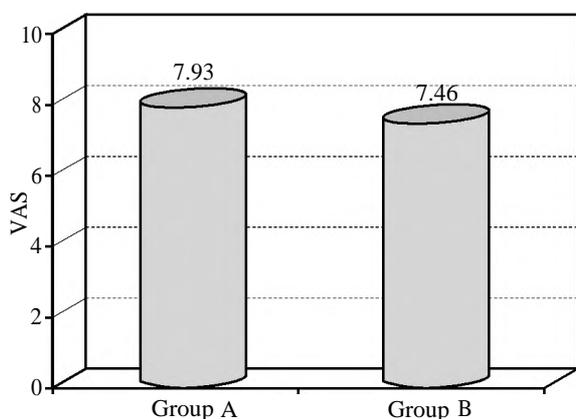


Fig. (3): Pretreatment mean values of VAS of both groups (A and B).

- Post treatment mean values of VAS of both groups (A and B):

The mean \pm SD VAS post treatment of group A was 5.6 ± 0.73 and that of group B was 6.73 ± 1.57 . The mean difference between both groups was -1.13 . There was a significant decrease in the VAS of group A compared with that of group B post treatment ($p = 0.01$) (Table 4, Fig. 4).

Table (4): *t*-test for comparison between post treatment mean values of VAS of both groups (A and B).

	VAS X \pm SD	MD	<i>t</i> - value	<i>p</i> - value	Sig
Study group	5.6 ± 0.73	-1.13	-2.51	0.01	S
Control group	6.73 ± 1.57				

X: Mean. MD: Mean difference.
p-value: Probability value. SD \pm : Standard deviation.
t-value: Unpaired *t*-value. S: Significant.

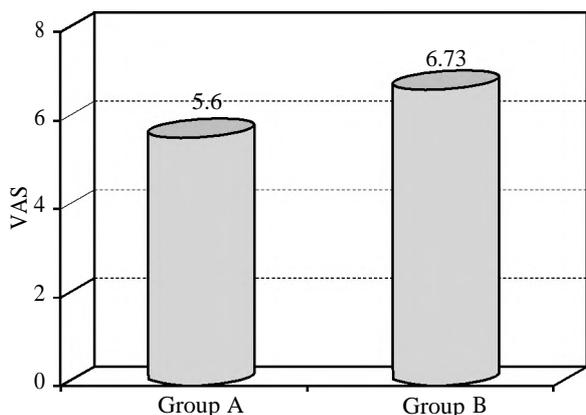


Fig. (4): Post treatment mean values of VAS of both groups (A and B).

2- Results of statistical analysis of 5-D itch scale:

- Pre and post treatment mean values of 5-D itch scale of group A:

The mean \pm SD 5-D itch scale pre treatment of group A was 20.33 ± 2.28 and that post treatment

was 16.33 ± 1.71 . The mean difference between pre and post treatment was 4 and the percent of change was 19.67%. There was a significant decrease in the 5-D itch scale of group A post treatment compared with that pre treatment ($p=0.0001$) (Table 5, Fig. 5).

Table (5): Paired *t*-test for comparison between pre and post treatment mean values of 5-D itch scale of group A.

	5-D itch scale X \pm SD	MD	% of change	<i>t</i> - value	<i>p</i> - value	Sig.
Pre treatment	20.33 ± 2.28					
Post treatment	16.33 ± 1.71	4	19.67	10.95	0.0001	S

X: Mean. MD: Mean difference.
p-value: Probability value. SD \pm : Standard deviation.
t-value: Paired *t*-value. S: Significant.

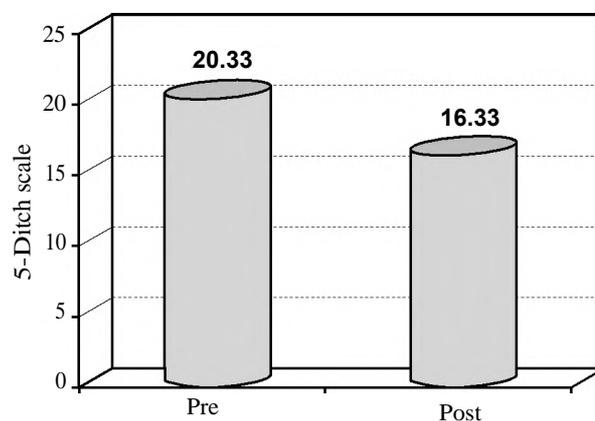


Fig. (5): Pre and post treatment mean values of 5-Ditch scale of group A.

- Pre and post treatment mean values of 5-Ditch scale of group B:

The mean \pm SD 5-D itch scale pre treatment of group B was 19.46 ± 2.5 and that post treatment was 18.53 ± 3 . The mean difference between pre and post treatment was 0.93 and the percent of change was 4.77%. There was a significant decrease in the 5-D itch scale of group B post treatment compared with that pre treatment ($p=0.002$) (Table 6, Fig. 6).

Table (6): Paired *t*-test for comparison between pre and post treatment mean values of 5-Ditch scale of group B.

	5-D itch scale X \pm SD	MD	% of change	<i>t</i> - value	<i>p</i> - value	Sig.
Pre treatment	19.46 ± 2.5					
Post treatment	18.53 ± 3	0.93	4.77	3.76	0.002	S

X: Mean. MD: Mean difference.
p-value: Probability value. SD \pm : Standard deviation.
t-value: Paired *t*-value. S: Significant.

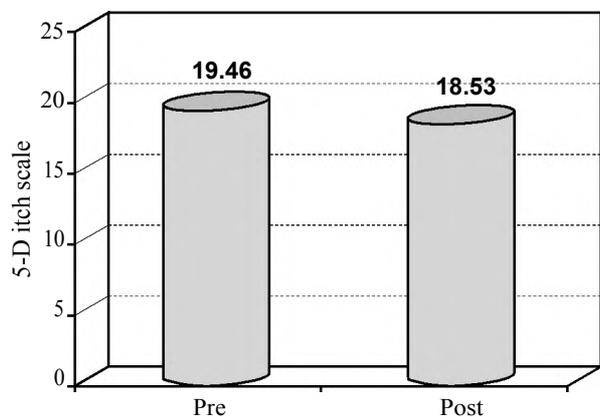


Fig. (6): Pre and post treatment mean values of 5-D itch scale of group B.

- Pre treatment mean values of 5-D itch scale of both groups (A and B):

The mean \pm SD 5-D itch scale pre treatment of group A was 20.33 ± 2.28 and that of group B was 19.46 ± 2.5 . The mean difference between both groups was 0.87. There was no significant difference in the 5-D itch scale between both groups pre treatment ($p = 0.33$) (Table 7, Fig. 7).

Table (7): *t*-test for comparison between pre treatment mean values of 5-D itch scale of both groups (A and B).

	5-D itch scale $X \pm SD$	MD	<i>t</i> -value	<i>p</i> -value	Sig
Group A	20.33 ± 2.28				
Group B	19.46 ± 2.5	0.87	0.99	0.33	NS

X : Mean. MD : Mean difference.
p-value: Probability value. SD \pm : Standard deviation.
t-value : Unpaired *t*-value. NS : Non significant.

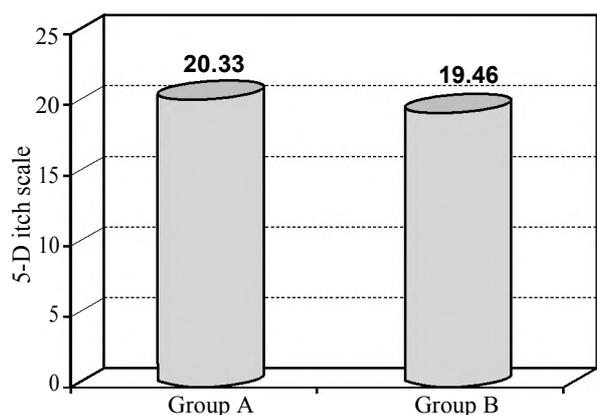


Fig. (7): Pre treatment mean values of 5-D itch scale of both groups (A and B).

- Post treatment mean values of 5-D itch scale of both groups (A and B):

The mean \pm SD 5-D itch scale post treatment of group A was 16.33 ± 1.71 and that of group B was 18.53 ± 3 . The mean difference between both

groups was 2.2. There was a significant decrease in the 5-D itch scale of group A compared with that of group B post treatment ($p=0.02$) (Table 8, Fig. 8).

Table (8): *t*-test for comparison between post treatment mean values of 5-D itch scale of both groups (A and B).

	5-D itch scale $X \pm SD$	MD	<i>t</i> -value	<i>p</i> -value	Sig.
Group A	16.33 ± 1.71				
Group B	18.53 ± 3	-2.2	-2.46	0.02	S

X : Mean. MD : Mean difference.
p-value: Probability value. SD \pm : Standard deviation.
t-value : Unpaired *t*-value. S : Significant.

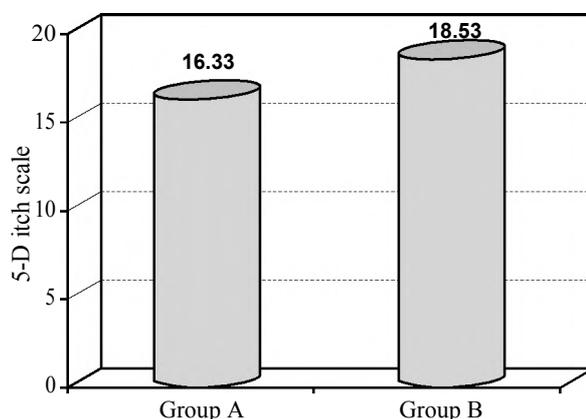


Fig. (8): Post treatment mean values of 5-D itch scale of both groups (A and B).

Discussion

The present study was designed to investigate the effect of narrow band ultraviolet B on renal pruritus in patients with chronic kidney disease.

Renal pruritus is one of the most frequent symptoms of dermatologic disorders in chronic kidney disease patients undergoing dialysis. It can cause the psychosocial and emotional well-being as well as the overall health-related quality of life of the patients. The hemodialysis patients with extreme pruritus were more like to have a high mortality rate, and suffer from sleep disturbances, depression or chronic subclinical inflammation. There is no confirmed evidence that renal pruritus can be caused by a single factor, whereas many metabolic factors have been implicated in the pathogenesis of pruritus, for example, hypercalcemia, hyperphosphatemia, secondary hyperparathyroidism, and hypermagnesemia [12].

Due to marked complexity of pathogenesis and associated comorbidities, the treatment of uremic pruritus remains challenging, despite the availability

of different modalities. Managing renal pruritus begins with precautions to avoid factors that can exacerbate the itch, such as contact with irritant substances, hot and spicy food, hot and alcoholic beverages, and negative stress, and by encouraging to moisturize the skin to reduce skin dryness. It is recommended to use mild, non-alkaline cleansers and to bath in lukewarm water for no more than 20 minutes. Soft clothing and frequent application of emollients are also beneficial [13].

Ultraviolet phototherapy exerts its biological effects in dermatologic disorders through several mechanisms. These mechanisms include apoptosis of inflammatory cells, inhibition of Langerhans cells, alteration of cytokine production, antimicrobial activity, improving skin barrier, and positive effect on vitamin D balance. UV treatment of renal pruritus result in decrease of neuropeptides from sensory nerve fiber resulting in inhibition of itch. Impairment of sensory innervation may also contribute to a reduced histamine released from mast cells and sensory nerve fibers conducting itch. The pruritogenic effect is partially mediated by histamine released from mast cell degranulation. It has been shown that NB-UVB induce apoptosis in mast cell. UVB phototherapy of patient with renal pruritus has been shown to significantly deplete cutaneous mast cells with subsequent reduction of pruritus intensity [14].

This study was conducted on thirty patient with renal pruritus. Their ages ranged from 40-60 years. They were selected from Hemodialysis Unit of Mansura University Hospitals.

Patients were randomly assigned in to two equal groups: Group (A) composed of 15 patients who received narrow band ultraviolet B 3 times/week for 6 weeks in addition to their medical treatment (oral antihistaminic and topical emollients) and group (B) composed of 15 patients who received only their medical treatment(oral antihistaminic and topical emollients).

Visual analogue scale (VAS) and 5-Ditch scale were assessed to both groups prior to and after 6 weeks of ultraviolet radiation using ultraviolet cabinet.

The results of this study revealed significant decreasing of VAS and 5-D itch scale in ultraviolet therapy group (group A) that agreement with (Wang et al., [15]; Seckin et al., [10]; Ada et al., [16]; Szepietowski et al., [17]; Jiraskova et al., [18]).

Wang et al., [15]. Tested the efficacy of narrow-band ultraviolet B phototherapy in reducing renal

pruritus. A convenience sample of 42 hemodialysis patients with pruritus was recruited from hemodialysis units of a general hospital. Two groups were created according to the dates of hemodialysis. The intervention participants received narrowband ultraviolet B phototherapy three times a week for two weeks. The control participants were maintained on their prior pruritus treatment. The pruritus intensity was measured with a numerical rating scale at baseline and on alternating days for seven times. The generalized estimating equation showed statistically significant group-by-time interactions in pruritus intensity. Using the control group as the reference group and baseline as the reference time, the intervention group had significantly lower pruritus intensity than the control group: 3.14 ($p < 0.001$) at time seven, 1.71 ($p < 0.0001$) at time six and 1.24 at time five ($p < 0.001$). The group-by-time interactions were statistically significant after four sessions of narrowband-UVB irradiation. The study findings support the efficacy of narrowband ultraviolet B phototherapy in alleviating renal pruritus.

Seckin et al., [10] studied 17 end-stage renal disease (ESRD) patients and found that eight-week NB-UVB phototherapy significantly relieved pruritus. The NB-UVB was given three times a week, with a starting dose of 150 mJ/cm² or 200 mJ/cm² based on patients' skin types and then increased by 20% each session. The patients' mean visual analogue scale (VAS) scores decreased from 8.2 (SD=1.5) to 3.6 (SD=0.3), corresponding to a 54.2%, 95% CI (32.6,75.9), change from baseline.

Ada et al., [16] investigated the effects of six-week NB-UVB phototherapy for 20 uremia patients. The irradiation was administered three times a week. Pruritus intensity significantly decreased by 70.8%, 95% CI (45.9,95.7), in patients (n=10) who completed 18 sessions of phototherapy and decreased by 69.3%, 95% CI (47.1-91.4), in patients (n=9) who completed only part of the phototherapy (M=3 weeks, ranging from 1-5 weeks).

Szepietowski et al., [17] tested the percentage mast cell apoptosis after exposure to ultraviolet B. data that both broad-band and narrow-band ultraviolet B irradiation are able to induce apoptosis in transformed mast cells in a dose-dependent manner at a time point of 24 hours. The difference between the number of apoptotic cells in all groups of ultraviolet B-irradiated cells and sham-exposed cells was highly significant ($p < 0.001$). Based on these findings, it is hypothesized that ultraviolet B induced mast cell apoptosis could be an important factor in phototherapy for the diseases dependent

on increased number of cutaneous mast cells, including uraemic pruritus.

Jiraskova et al., [18] studied the effect of ultraviolet radiation on uremic pruritus. Fifteen patients were exposed to UVB radiation for 6 weeks. Ten of the treated patients reported a marked regression of pruritus, three a slight relief and two of them did not notice any change in the intensity of itching. The study concluded that UVB is probably highly effective on inhibition of pruritus.

On the other hand, the results of this study contradict with (Ko et al., [20]).

Ko et al., [19] in a randomized clinical trial (n=10 exercise group, n=11 control group), compared a six week NB-UVB phototherapy with a time-matched UVA control condition. NB-UVB was administered three times a week. At the post-test, there was no between-group difference in pruritus intensity. Both groups had significant reduction in pruritus intensity. The VAS score decreased by 3.53 (95% CI 602-1.03) in the NB-UVB group and by 338 (95% CI: 5.54-1.21) in the control group. They concluded that NB-UVB phototherapy had no significant effect on renal pruritus and suggested the pruritus reduction in both groups were mostly likely due to a placebo effect of good doctor-patient relationships.

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فاعلية الأشعة فوق البنفسجية الضيقة النطاق ب على الحكة الكلوية فى مرضى الكلى المزمن

الهدف من البحث: أجرى هذا البحث لتقييم تأثير الأشعة فوق البنفسجية الضيقة النطاق ب على الحكة الكلوية فى مرضى الكلى المزمن. مواد وأساليب البحث: أجريت هذه الدراسة على ثلاثين مريضاً ممن يعانون من الحكة الكلوية وقد تراوحت أعمارهم بين الأربعين والستين عاماً، تم اختيارهم من وحدة الغسيل الكلوى بمستشفيات جامعة المنصور بالدقهلية وقد تم تقسيمهم عشوائياً إلى مجموعتين متساويتين: ١- المجموعة الأولى (مجموعة الدراسة): أحتوت هذه المجموعة على خمس عشر مريضاً ممن تلقون العلاج بالأشعة فوق البنفسجية الضيقة النطاق ب بواقع ثلاث جلسات أسبوعياً وذلك لمدة ستة أسابيع إلى جانب أخذهم للعلاج الطبى والذى يشمل مضادات الهستامين عن طريق الفم والمطريات الموضعية. ٢- المجموعة الثانية (المجموعة الضابطة): أحتوت هذه المجموعة على خمس عشر مريضاً ممن لم يتلقوا أي علاج سوى علاجهم الطبى والذى يشمل مضادات الهستامين عن طريق الفم والمطريات الموضعية.

النتائج: وقد أظهرت النتائج ما يلى:

هناك مزيد من التحسن فى المرضى الذين عولجوا بالأشعة فوق البنفسجية الضيقة النطاق ب (أ) أكثر من هؤلاء المرضى الذين لم يتلقوا العلاج الضوئى وكانوا يأخذون فقط علاجهم الدوائى (ب) كما يتضح من نتائج المقياس البصرى التناظرى ومقياس الحكة الجلدية لذا أثبتت النتائج أن الأشعة فوق البنفسجية الضيقة النطاق ب طريقة فعالة فى تقليل حدة الحكة الكلوية فى مرضى الكلى المزمن.