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ORIGINAL ARTICLE

Retrospective Study

Role of narrow band ultra violet radiation as an add-on therapy in peritoneal dialysis patients with refractory uremic pruritus

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Abstract

AIM

To assess the role of narrow band ultraviolet B (UVB) as a treatment option in peritoneal dialysis patients with refractory uremic pruritus.

METHODS

In this retrospective study, 29 adult patients with end stage renal failure on peritoneal dialysis, and who had refractory uremic pruritus, were given narrow band UVB radiation as an add-on therapy to standard care for a duration of 12 wk. The response to the pruritus was assessed both weekly and at the end of the study period using a visual analogue score (VAS).

RESULTS

The average VAS score at the end of the study was 3.14 ± 1.59, which was significant compared to the baseline value of 7.75 ± 1.02 ($P < 0.05$). Improvements in symptoms were noted in 19 out of 21 (90.4%) patients. However, relapse occurred in six out of the 19 patients who responded. The dropout rate was high during the study period (33.3%).

CONCLUSION

Narrow band UVB is effective as an add-on therapy in peritoneal dialysis patients with refractory uremic pruritus. However, the present regime is cumbersome and patient compliance is poor.

Key words: Narrow band ultraviolet radiation; Uremic

pruritus; Peritoneal dialysis; Visual analogue score; Retrospective study

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Core tip: Uremic pruritus is a very distressing condition commonly seen in patients with advanced renal failure. Patients respond poorly to the currently available treatment regime. Narrow band ultraviolet (NUV-B) radiation is a treatment option in patients with refractory symptoms. In this study, we selected patients on peritoneal dialysis who had refractory pruritic symptoms, and used NUV-B as an add-on therapy to the standard medical care for a period of 12 wk. We found that using NUV-B improved symptoms in more than 90% of patients. However, the present regime used is not patient-friendly and compliance is poor.

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INTRODUCTION

Uremic pruritus is a very common and troublesome complication seen in patients with advanced chronic kidney disease[1-4]. The pathophysiology is complex, and many factors have been identified, including skin dryness[5,6], hyperparathyroidism[7,8], calcium phosphate deposition[9,10], imbalances between mu and kappa opioid receptors[11,12] and systemic inflammation. Anemia, inadequate dialysis, elevated serum magnesium and aluminum levels, and hepatitis C infection are also believed to have some contributing effects. However, the causes remain unexplained in many cases. There are strong associations of uremic pruritus with depressive symptoms and poor sleep quality. The pruritus is sometimes severe and refractory to treatment. Narrow band ultraviolet B (NB-UVB) phototherapy is one therapeutic option in these difficult cases. NB-UVB decreases the proinflammatory cytokine levels and induces mast cell apoptosis. In this study, we aim to investigate the role of NB-UVB as an add-on therapy to the standard treatment that is used in treating severe uremic pruritus in peritoneal dialysis patients.

MATERIALS AND METHODS

This retrospective study was conducted in the Department of Dermatology at the Jawaharlal Nehru Institute of Medical Sciences Imphal, a tertiary referral center in northeastern India. Adult end-stage renal disease patients on peritoneal dialysis with refractory uremic pruritus were included in the study. The patients were recruited from the nephrology units of three hospitals in Imphal from September 2011 to September 2017. The selected patients were referred to the Dermatology Department at the Jawaharlal Nehru Institute of Medical Sciences Imphal for NB- UVB therapy.

Inclusion criteria

In order to be eligible for inclusion in this study, patients had to be older than 18 years of age, have end-stage renal disease, be on peritoneal dialysis as their treatment modality, and have refractory uremic pruritus.

From September 2011 until September 2017, 29 patients satisfied the criteria. Uremic pruritus was defined as pruritus developing in patients with chronic kidney disease in the absence of other systemic, dermatological disorder or psychological factors. Refractory uremic pruritus was defined as uremic pruritus not that was not responsive to any of the two agents known to relieve the symptoms over a 4 wk period. These agents included topical emollients, topical capsaicin, antihistamines, pregabalin, gabapentin and tricyclic antidepressants.

Exclusion criteria

Patients with a prior history of photosensitivity, and other prior dermatological diseases that can cause pruritus, were excluded from this study.

Protocol: The patients were administered NB-UVB therapy every other day, three times per week for a total of 12 wk. They were started at a dose of 270 mJ/cm^2, and then increased by 15% at each visit. If patients had asymptomatic erythema after the session, then treatment was continued at the same dose. The dose was reduced by 15% if the patient developed erythema with minimal pain/itchiness. If the patient developed painful erythema or bullous lesions, treatment was restarted at one-third of the dosage. Phototherapy was administered using "Derma India, Chennai Lightning cubicles PUVA", which is equipped with 24 UVA lamps that emit a radiation spectrum of 320-400 nm with a maximum of 366 nm, and 24 UVB lamps that emit a radiation spectrum of 290-320 nm with a maximum of 300 nm.

The patients were allowed to continue with their previous medications/agents for uremic pruritus during the study period. A peritoneal adequacy test was performed in all patients upon entry into the study. Serum calcium, phosphate, intact parathyroid hormone, iron and hemoglobin profiles were evaluated in all patients.

A visual analogue scale (VAS) (0 = no pruritus; 10 = most severe pruritus) was used to identify the intensity of itch. VAS was measured at baseline and then weekly until the end of the 12th week. After completion of the treatment protocol, VAS was then measured monthly during the follow-up period.

Table 1 Baseline characteristics of the patients

Age (yr)	56.17 ± 15.65
Sex (male/female)	18/11
Hemoglobin (g/L)	9.99 ± 0.99
Corrected calcium (mg/dL)	8.92 ± 1.1025
Phosphate (mg/dL)	4.46 ± 1.35
Intact parathyroid hormone (pg/mL)	132.28 ± 176.63
Mean Kt/V	1.77 ± 0.11
No. of patients with weekly Kt/V > 1.7	19
Skin phototype	IV-20, V-9
Other agents used for pruritus	
Topical emollient	
Topical capsaicin	
Oral anti histaminics: Fexofenadine	
Pregabalin	
Gabapentin	
Amitryptilline	

The outcomes were grouped into the following: (1) Complete responders: defined as a VAS score of zero at the end of the study period; (2) Partial responders: defined as a VAS score between one to five at the end of treatment, and with a final VAS score less than the value at baseline; and (3) Non-responders: a VAS score greater than five at the end of the treatment period.

Relapse was defined as a VAS score greater than five after previously showing a complete or partial response.

After the completion of the treatment protocol, patients were followed-up on a monthly basis for another 6 mo. During the follow-up period, patients were assessed for relapse of the pruritus. VAS scores were recorded during these visits. A feedback form was also provided to the patient. This form allowed them to rate their experience with the treatment protocol and provide suggestions to improve their adherence.

Statistical analysis

Statistical analysis was performed using the SPSS 16 software. Continuous data were described as the mean ± SD, and categorical data by frequency and percentage. Paired *t*-tests were used to compare the mean VAS scores at baseline with those at the end of the study. A two-sided *P* score of < 0.05 was considered significant.

RESULTS

A total of 29 patients took part in this study. Seven patients dropped out during the treatment period. One patient died during this period. Baseline characteristics of the patients are shown in Table 1.

The mean age of the patients was 56 ± 15 years. The mean duration on peritoneal dialysis of these patients at the time of study was 10 ± 8 mo. The average baseline VAS for pruritus was 7.75 ± 1.02. At the end of the treatment period, the average VAS score was 3.14 ± 1.59, which was a significant drop from the baseline score ($P < 0.05$). Twenty-one patients completed the study, and 19 of them (90.4%) showed improvements in pruritus severity. Complete resolution of pruritus was noted in three patients (14.2%). Two patients (9.5%) continued to have persistent pruritus, with VAS scores greater than five (Table 2).

Follow-up data were available for 14 patients. The mean VAS score at the end of the follow-up period was 4.14 ± 2.85. Six patients relapsed with pruritus, with VAS scores greater than five. The mean time to relapse was approximately 4.2 ± 2.99 mo.

No significant adverse effects attributable to NB-UVB were identified.

DISCUSSION

Uremic Pruritus is a fairly common entity in patients with advanced renal failure, including patients on hemodialysis as well as peritoneal dialysis. In a recent study in Chinese patients, the prevalence of uremic pruritus in patients on peritoneal dialysis was approximately 62.5%[13].

The usual protocol followed in managing patient with uremic pruritus includes optimization of the dialysis dosage, optimizing treatment of hyperparathyroidism, hyperphosphatemia and anemia. Initially, patients are usually managed with emollients and topical analgesics for symptomatic measures. Many of these patients eventually require systemic medications, such as anti-histamines, pregabalin, gabapentin, and anti-depressants. Hemoperfusion has been used in combination with hemodialysis for hyperparathyroidism and pruritus in hemodialysis patients[14]. A small population of patients continue to have persistent symptoms in spite of all these measures. Phototherapy may be tried as a treatment modality in these cases.

In a small open pilot study, Ada *et al* reported a satisfactory response to NB-UVB in patients with uremic pruritus[15]. The randomized clinical study by Ko *et al*[16] showed significant improvement in the pruritus intensity, however the beneficial effect was marginal when compared to the control group that received long-wave UVA radiation.

In our study, we noted that NB-UVB phototherapy was helpful as an add-on therapy in relieving symptoms of uremic pruritus in patients on peritoneal dialysis. A previous randomized controlled trial by Ko *et al*[16] failed to show any substantial benefit compared to broadband UVA phototherapy. This lack of benefit was due to improvement in pruritus intensity in the control arm, which they attributed to the placebo effect. However, the population studied in that trial differs from that of our study. In our study, we included only patients with end-stage renal disease who were on peritoneal dialysis. Conversely, the study by Ko *et al*[16] used a mixed population of patients, including those with chronic kidney disease on conservative treatment. Only three patients in that study were on peritoneal dialysis. Another important difference from that study is the duration of the treatment period. Per our protocol, the total duration

Table 2 The baseline and weekly visual analogue assessment scores for pruritus

	Baseline	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12
Mean VAS score	7.75 ± 1.02	7.55 ± 1.02	7.48 ± 0.82	7.03 ± 0.68	6.37 ± 0.49	5.66 ± 0.55	5.53 ± 0.64	5.20 ± 0.70	4.87 ± 0.74	4.60 ± 0.72	3.04 ± 1.32	3.42± 1.63	3.14 ± 1.59
No. of patients	29	29	29	29	27	27	26	25	24	23	22	21	21

VAS: Visual analogue score.

of therapy was 12 wk compared to the six week time-span used in the randomized trial. The extended duration of our treatment is based on our preliminary experience with such patients, where we noted a more significant improvement in symptoms when they received a more prolonged course of treatment.

The pathophysiology involved in uremic pruritus is very complex and multifactorial. Multiple hypotheses have been proposed, including the potential involvement of anemia, xerosis, hyperparathyroidism, hyperphosphatemia, inadequate dialysis, imbalance of opioid receptors, and inflammation. Some of the factors that contribute to pruritus in non-dialysis patients may not be applicable in patients who are already on peritoneal dialysis. The response of uremic pruritus to phototherapy may differ in the peritoneal dialysis population when compared to patients on hemodialysis. The beneficial effects of NB-UVB is believed to be attributable to the induction of mast cell apoptosis and the reduction in proinflammatory cytokine levels[17].

In our study, the mean hemoglobin levels (9.99 ± 0.9) are very near the target set by KDIGO[18]. The serum phosphate levels (mean value 4.44 mg/dL) and intact parathyroid levels (mean value 132.28 pg/mL) were also reasonable for patients on dialysis. Nineteen out of the 21 patients who completed the study had adequate small solute clearance (weekly kt/v > 1.7), suggesting that factors other than inadequate dialysis played a significant role in the pathogenesis of uremic pruritus in our patients.

We noted that using NB-UVB as an add-on therapy was effective in our patients. The mean VAS score improved from a baseline score of 7.75 ± 1.02 to 3.14 ± 1.59 by the end of therapy. Complete resolution of pruritus was noted in three patients (14.2%). In two patients (9.5%), no significant improvements were noted. Six of the patients who showed an improvement in pruritus ultimately relapsed (31.5%).

The beneficial effects of the phototherapy session set in by the 3rd week, and the effect became more pronounced after the end of the 7th week. The mean VAS score at the end of six weeks was 5.53 ± 0.64, which means that many of these patients would have been classified as non-responders if they had received the 6 wk protocol, as in the previous randomized trial. The mean VAS score at the end of the 6 mo follow-up was 4.14 ± 2.85, which was significantly lower than the baseline VAS score ($P < 0.001$).

Our study is limited by its retrospective nature. Although the population studied here is uniform, it is also small. We noted that it was difficult for the patients to strictly abide by the three times per wk for 12 wk UVB protocol. Upon reviewing the feedback forms, we realized that our patients found the treatment regime to be cumbersome, and many were not willing to enroll in a repeat course of such treatment sessions in the future. This was in spite of the short duration of each session, usually lasting less than two to 3 min. Many of the patients found the frequent visits to the hospital to be very inconvenient. Transportation was also a big hindrance, as many of these patients cannot drive and thus arranging logistical support to bring them to the hospital three times a wk for 12 wk becomes an issue. It is noted that the duration of the overall treatment protocol was longer compared with previous studies. As such, one might consider a slightly shorter duration of NB-UVB treatment (*e.g.,* twice per week for eight to 10 wk, or three times per week for 8 wk).

Many questions still remained unanswered at the end of this study. The treatment, even if effective, does not offer long-term protection. Relapse occured in nearly a third of the patients. The optimal treatment duration and frequencies of the session are not known. As such, we need to come up with a large well-designed randomized controlled trial comparing different treatment regimes in order to come up with the most effective yet acceptable regime.

In conclusion, using NB-UVB as an add-on therapy to standard agents in refractory uremic pruritus on peritoneal dialysis is effective in reducing the intensity of itching. However, there is a chance of relapse after discontinuation of the phototherapy. The 12 wk treatment regime used in this study is cumbersome and patient acceptance is poor.

ARTICLE HIGHLIGHTS

Research background

Uremic pruritus is a common and troublesome entity in patients on peritoneal dialysis. The presence of pruritus affects both sleep quality and overall lifestyle, which can lead to depressive symptoms and mood disorders. In patients with difficult-to-treat pruritus, narrow band ultraviolet B (NB-UVB) can be tried as a treatment option. There is only one randomized controlled trial that has compared the role of NB-UVB in uremic pruritus. There is very limited data regarding the use of NB-UVB in the peritoneal dialysis population. There is therefore an urgent need to identify the effectiveness of such a treatment modality in the peritoneal dialysis population.

Research motivation

With the limited data available, there is no clear-cut consensus regarding the role of NB-UVB in peritoneal dialysis patients who have severe pruritus. The most effective and optimal duration of treatment is also not clear. A previous randomized trial had used a course of three times a week for 6 wk. However, that study mixed in a population of chronic kidney disease patients and also included patients on hemodialysis, peritoneal dialysis, as well as patients who were treated conservatively and had not been initiated on dialysis. There were only three patients in this study who were on peritoneal dialysis, so the results therefore cannot be extrapolated to the peritoneal dialysis population. In this study, we selected a homogenous population of patients with end-stage renal disease who were on peritoneal dialysis with severe uremic pruritus, and used NB-UVB as an add-on therapy to the standard treatment.

Research objectives

The purpose of our study was to assess the effectiveness of NB-UVB as an add-on therapy to standard treatment in peritoneal dialysis patients with refractory uremic pruritus. We included a follow-up 6 mo post-treatment completion to assess for relapse. Patients were also given a feedback form to highlight their experience with the treatment protocol and solicit their suggestions to improve the quality of treatment.

Research methods

This is a retrospective study where peritoneal dialysis patients with refractory uremic pruritus were put on a 12 wk course of NB-UVB, in addition to their standard treatment. We used visual analogue scale (VAS) to record the intensity of pruritus, which was measured during each visit. After the completion of their treatment protocol, patients were followed-up on a monthly basis for six months, and their VAS scores were measured during these visits. The patient feedback forms were also collected during these follow-up visits.

Research results

In this study, we noted that the mean VAS score improved from a baseline of 7.75 ± 1.02 to 3.14 ± 1.59 by the end of treatment. Nineteen out of the 21 patients who completed the study had improvement in symptoms. In three patients (14.2%), complete resolution of pruritus was noted. Two patients (9.5%) continued to have persistent pruritus, with VAS scores greater than five. Six (31.5%) of those patients who showed improvement in pruritus ultimately relapsed. The mean VAS score at the end of the 6 mo follow-up was 4.14 ± 2.85, which was significantly lower than the baseline VAS score ($P < 0.001$).

Research conclusion

In this study, we found that NB-UVB therapy is effective as an add-on therapy in difficult-to-treat patients with uremic pruritus in the peritoneal dialysis population. In our study, we used a 12 wk treatment protocol that showed effective results. We noted that the response at 6 wk was suboptimal, and many of our patients would have been classified as non-responders if our treatment was confined to 6 wk period. However, patient compliance was poor, and the frequent visits to the hospital for treatment became an issue when we used the 12 wk regime. We therefore need to come up with an effective treatment regime that will also be acceptable to patients.

Research perspectives

Future studies should try alternative treatment regimes, such as two times per wk for 10 wk, or three times per wk for 8 wk.

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