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Original Article

A study to evaluate efficacy and safety of broadband UVB in the treatment of uraemic pruritus

評定寬頻紫外線 B 治療尿毒症瘙癢的有效性及安全性研究

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Uraemic pruritus is poorly understood and treatment is often difficult. Broadband Ultraviolet B (BBUVB) therapy has been shown to be effective in controlled trials in Caucasians. A double-blind randomised controlled trial comparing BBUVB with Ultraviolet A (UVA) as control was carried out on 19 Chinese patients who had skin types III or IV. These patients suffered from uraemic pruritus not controlled with topical steroid and oral antihistamines. All patients were screened to exclude other causes of the pruritus. Ten patients received BBUVB while nine patients received UVA. One patient in the BBUVB group died of a stroke during study period and three patients from the UVA group defaulted and failed to complete the study. Pruritic symptoms measured by pruritic score and self assessment score by visual analogue scale were recorded. Fifteen patients (BBUVB N = 9, UVA N = 6) had completed the study. All patients of the BBUVB group and two from the UVA group showed a more than 50% reduction in pruritic score from week 0 to week 6. The response rate for patients in the BBUVB group was shown to be better and statistically significant by Fisher's Exact Test ($p = 0.02198$) and by Wilcoxon Rank Sum Test ($p < 0.05$). The visual analogue self assessment scale correlated well with change in the pruritic score. Treatment was well tolerated without short-term side-effects. We conclude that twice weekly BBUVB therapy for six weeks is effective in controlling uraemic pruritus.

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目前對尿毒症瘙癢所知不多，治療亦困難。在白種人中，寬頻紫外線B療法經對照試驗研究証實有效。本研究在19名III型及IV型皮膚的華人中，以紫外線A作對照，作雙盲對照試驗，比較寬頻紫外線B的療效，患者均患尿毒症瘙癢且經局部類固醇及口服抗組胺藥治療無效，其他致癢因素經已排除。10名患者接受寬頻紫外線B治療，9名接受紫外線A治療。寬頻紫外線B組中1人因中風死亡; 紫外線A組中3人因退出而未完成評定。以瘙癢評分及視覺對應等級自我評分記錄並評定其瘙癢症狀。15名患者（寬頻紫外線B組9人，紫外線A組6人）完成研究。自0至6週，全數寬頻紫外線B組患者及2名紫外線A組患者的瘙癢評分減少50%。費希爾準確試驗（P=0.02198）及威氏總秩試驗（P<0.05）顯示寬頻紫外線B組療效較好，且具統計學意義。視覺對應等級自我評分與瘙癢評分的相關性良好。無短期副作用，治療耐受性好。我們認為每週兩次、為期六週的寬頻紫外線B能有效控制尿毒症瘙癢。

Keywords: Broadband UVB, Uraemic Pruritus

關鍵詞：寬頻紫外線B，尿毒症瘙癢

Introduction

Generalised pruritus is a common and often severe among uraemic patients.[1] Treatment modalities that include oral cholestyramine, anti-histamines, charcoal, heparin, lidocaine, parathyroidectomy and recent use of erythropoietin produced inconclusive result. Broadband ultraviolet B (BBUVB) phototherapy has been shown by several small studies to be effective in ameliorating pruritus in uraemic patients.[2]

Objectives

To investigate the efficacy and adverse effects of BBUVB therapy in uraemic Chinese patients who are on dialysis with pruritic symptoms not controlled by topical steroid and oral antihistamine treatment.

Patients and methods

Uraemic patients putting on dialysis with pruritic symptoms for at least two months and severe enough to disturb sleep or daily activities and unresponsive to oral anti-histamines and topical treatment were enrolled into the study. Exclusion criteria include pre-existing dermatological diseases, obstructive liver disease, uncontrolled hypercalcaemia, history of systemic lupus erythematosus and photo-sensitivity that precluded phototherapy.

Study design

This is a prospective study carrying out in a renal unit of a regional general hospital. Patients were randomly assigned to receive twice weekly either BBUVB or ultraviolet A (UVA) (as a control) for a period of six consecutive weeks. Each patient was assessed after each phototherapy session for side effects and determination of subsequent irradiation dosage. Pruritic symptoms were assessed by a single investigator who was blind-folded for the type of phototherapy given to the patients. The study was approved by the Hospital Authority Ethics Committee. Informed consent was given to patient who agreed for enrollment into the study.

Light sources

Phototherapy was delivered by Waldmann Lichttechnik UV100 Irradiation Unit which was equipped with lamps delivering either BBUVB or UVA. The UVA lamps gave a radiation spectrum of 315-400 nm while the BBUVB lamps gave a radiation spectrum of 285-350 nm.

Treatment protocol

All patients were subjected to a phototest to determine their individual Minimal Erythema Dose (MED). After determining the MED, each patient would receive timed phototherapy starting at 80% of his MED; with successive 10-20% increment of irradiation time at the next treatment until faint erythema was reached. All patients received six weeks' course of twice weekly whole body phototherapy with coverage of face and genitalia. All anti-pruritic treatment was stopped except moisturising creams.

Outcome measures

1. *Pruritic score*
   Pruritic score validated in haemodialysis and CAPD patients by Mettang et al in 1990 was used.[3] The score was based on summation of severity and distribution of pruritic symptoms during the day and disturbance to sleep at night. It is a product of Severity score and Distribution score and is done twice on an average day and added to the Sleep score. The severity of itch is rated 1 point for itching without scratching, 2 points for scratching without excoriations, 4 points for scratching which is interminable or accompanied by excoriations, and 5 points for itching causing total restlessness. Distribution score is given 1 point for itching at less than three locations, 2 points for more than two locations and 3 points when itching is generalised. The sleep score measured the magnitude of sleep disturbance due to itching; 2 points were given to each episode of waking up and up to a maximum of 10 points can be allocated. This will give a Pruritic score range from 2 to 40. The Pruritic score was taken at baseline just before start of phototherapy and then at every 2 weeks during treatment by a single investigator.

2. *Visual analogue scale*
   This is the patient perceived visual analogue scale from zero (no pruritus) to 10 (most pruritic), taken at baseline and at the end of the 6 weeks phototherapy.

3. *Statistics*
   Mean ± standard error of means were used to express numerical data. Student-t 2-tails test were used to compare the means. Fishers exact test were used to compare nominal groups. Pearson correlation was performed to compare the change in Pruritic Scores and the patient perceived visual analogue score.

Results

Nineteen patients with 10 for BBUVB and 9 for UVA (control) were enrolled. Three patients from the UVA (control) group did not complete the study for unsatisfactory symptom relief. One patient in the BBUVB group died of stroke. Fifteen patients completed the six weeks phototherapy.

The age (51±2.58 vs 54±4.48 year), haemoglobin level (8.78±1.0 vs 7.35±0.53g/dl), calcium (2.35 ±0.55 vs 2.47±0.13 mmol/L) and the phosphate (1.98±0.11 vs 2.25±0.20 mmol/L) levels of the two groups were comparable (Table 1). Three patients from each group had significant secondary hyperparathyroidism as defined by the serum level of intact PTH above 5 times the upper limit of normal. Only one patient was given erythropoietin who also had thalassaemic trait. His haemoglobin level remained at around 7 g/dl during the study period. All patients except one in the control group were of the skin type III or IV.

All patients showed reduction in their Pruritic Scores at the end of the six weeks treatment (Figure 1). The percentage reduction in the pruritic scores showed a bimodal distribution. When more than 50% reduction in the pruritic score was taken as the definition for responder, nine out of nine patients in the BBUVB group and only two out of six in the control group were responders. Actually all responders had at least 70% reduction in their

Table 1. Clinical data of patients in BBUVB and UVA (Control) groups

	UVA	UVB	p-value
No. of patient	6	9	
Age (year)	54±4.48	51±2.58	P=0.5584
Hb (g/dl)	7.35±0.53	8.78±1.0	P=0.2973
Calcium (mmol/L)	2.47±0.13	2.35±0.05	P=0.5001
Phosphate (mmol/L)	2.25±0.20	1.98±0.11	P=0.2162
[Ca] x [PO4]	5.53±1.19	4.73±0.84	P=0.1510
Magnesium (mmol/L)	0.83±0.06	0.85±0.07	P=0.9746
iPTH (pmol/L)	51.82±26.75	21.08±4.90	P=0.2361
iPTH ≥5x	3	3	NS
Erythropoietin	0	1	NS
Skin type			
II	0	1	NS
III	5	5	NS
IV	1	3	NS

pruritic scores. The difference in the respond rate between the two groups were statistically significant (p=0.02198, Fisher exact test). Improvement in pruritic symptoms with BBUVB phototherapy was seen early in the course of treatment. Significant reduction of pruritic scores were shown starting from the second week and onward. There was a good correlation between the change in pruritic scores and the patient perceived improvement in pruritic symptoms (r=0.7) (Figure 2). During the mean follow up period of 8.3 months, four responders from the BBUVB group reported recurrence of pruritus after 3 months but the intensity was much milder.

Adverse effects included mild degree of suntan were seen in three patients (1 in BBUVB, 2 in UVA), and exacerbation of pruritus after the first one or two treatment sessions in four patients with two in each group. This symptom improved spontaneously with continuation of phototherapy.

Discussion

Uraemic pruritus is one of the most common and distressing symptoms for dialysis patients and it is not well understood. Various forms of treatment

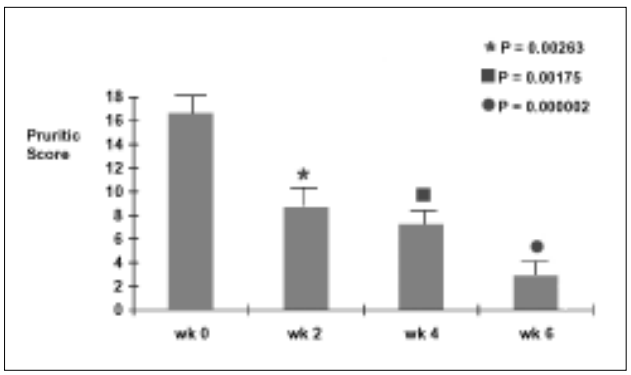

Figure 1. Pruritic scores in 9 patients receiving BBUVB.

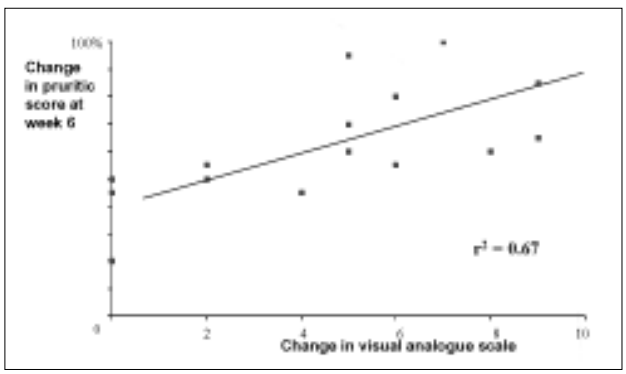

Figure 2. Correlation between pruritic score and visual analogue scale.

have been tried including systemic anti-histamines, IV lidocaine, parathyroidectomy, Ion binding resin, activated charcoal, erythropoietin and phototherapy. Evaluating efficacy of these treatment modalities need a comparable control group, blinded treatment and assessment methods, objective and reproducible grading of pruritic symptoms and a thorough dermatological assessment of each studied patients.

The use of recombinant erythropoietin in dialysis is getting more popular.[4] However, its anti-pruritic effects needs further evaluation. The use of oral activated charcoal has been shown to be effective for uraemic pruritus as reported by an Italian group.[5] However the large dose of activated charcoal at 6 g/day used reduces patient acceptability and possible drug interaction in this group of poly-pharmacy patients.

Phototherapy for treating uraemic pruritus was first reported by Gilchrest et al in 1977. Meta-analysis by Tan et al has shown that UVB phototherapy is the most effective treatment and others has shown that phototherapy gave the most lasting effect on completion of treatment.[6,7] Our study results are concordant with other studies. Although prolonged exposure to UVB especially at young age is known to associate with increased risk of developing non-melanoma skin cancers. However, in our study, patients only received less than 30 MEDs of BBUVB during a six weeks' course of phototherapy, it is therefore very unlikely that such phototherapy regime if given to uraemic patients will cause significant increase in risk of developing skin cancer.

With the advent of phototherapy equipment, light source cabinets can now be conveniently fitted into any dialysis units. However, a trained nurse to conduct and supervise phototherapy is important. Collaboration with dermatologist would be invaluable as other systemic causes of general pruritus need to be ruled out and phototherapy procedures supervised.

Conclusion

BBUVB is safe and effective in controlling moderate to severe uraemic pruritus in patients undergoing dialysis including CAPD patients. Initial exacerbation and subsequent recurrence of symptoms may occur but are usually mild. Relief of symptom is observed after two to three treatment sessions and the amelioration of itch can persist up to several months.

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