**Title: A Retrospective Review of Phototherapy in Children, at a Tertiary Paediatric Unit.**

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**Abstract:**

Purpose: To examine the efficacy, tolerability and safety of phototherapy in children, in whom there is currently a paucity of data.

Method: Retrospective review of children under 18 years who received narrowband UVB (NB-UVB), broadband UVB (BB-UVB) phototherapy or psoralen with UVA (PUVA) photochemotherapy between 2003-2017 at a tertiary Paediatric dermatology centre in Southampton, UK.

Results: 100 children aged 6-17 years were included. The majority of children had psoriasis (74), atopic dermatitis (10) or vitiligo (8), with others having rarer dermatoses. Grade 2 erythema or above occurred in 46% of all included children and 42% (36/86) of those receiving NB-UVB; however, grade 3 and 4 reactions were infrequent and only 3 children stopped treatment due to burning. NB-UVB was particularly effective in those with psoriasis; 55/65 (85%) significantly improved and 72% had not relapsed after 2 years. However, its effectiveness in atopic dermatitis was less convincing; in a small group of children 6/10 (60%) significantly improved, but 66% relapsed within 3 months.

Conclusions: Our analysis demonstrates that NB-UVB is effective in children with psoriasis and vitiligo, with potential to achieve extended periods of remission in psoriasis. Its usefulness in atopic dermatitis is less clear. The long-term safety of NB-UVB in children is still unknown, but it appears to be a well-tolerated treatment and should be considered in children for a variety of inflammatory dermatoses before progressing to immunosuppressive therapies.

**Introduction:**

Phototherapy is a well-established second-line therapy for a variety of dermatoses, including psoriasis, atopic dermatitis, vitiligo, polymorphic light eruption, pityriasis lichenoides chronica, lichen planus and cutaneous T-cell lymphoma. Whilst there is an abundance of efficacy and safety data for phototherapy in adults, this is lacking in children, especially for less common conditions.

We present a retrospective analysis of children at our centre in Southampton, UK who received phototherapy. We identified the clinical diagnosis treated and the type of phototherapy used, the number of children who experienced side-effects and where possible, assessed the effectiveness of the treatment by measuring response and relapse rates.

**Methods**:

All patients under the age of 18 years, who received NB-UVB or BB-UVB phototherapy or PUVA photochemotherapy between August 2003 and January 2017, at our centre in Southampton, UK, were identified using the electronic record system (HICCS). Patient demographics including age, sex and skin type were recorded (table 2).

The phototherapy machines used were Waldmann UV 7001 (NB-UVB), Waldmann UV 7002 (NB-UVB) and Waldmann UV 7001K (NB-UVB and UVA). The minimal erythema dose (MED) or minimal phototoxic dose (MPD) was assessed in all patients before starting treatment, except those with vitiligo who followed the departmental protocol starting at 0.04 J/cm2. Treatment was commenced at 70% of the MED in children with psoriasis and atopic dermatitis. NB-UVB was administered 3 times a week and bath PUVA was administered twice a week. Dose increments of 10% for atopic dermatitis and 20% for psoriasis vulgaris were used for all forms of phototherapy. Episodes of erythema were recorded using the departmental erythema grading tool shown in table 1. Written consent was obtained by experienced phototherapy nurses, who also recorded the global physician assessment for each patient completing treatment. This was recorded as either: clear/nearly clear; significant improvement; moderate improvement; mild improvement; or no improvement/worse. Topical therapy was continued during phototherapy.

**Results:**

Of the 100 patients included, 74 (74%) had psoriasis, 13 (13%) had atopic dermatitis, 8 (8%) vitiligo; the remaining conditions treated are shown in table 2. Skin types I-III were most frequent in this cohort (87%). 87 (87%) patients received NB-UVB. Responses to NB-UVB and mean cumulative dose (MCD) are recorded in table 3.

*Psoriasis:*

74 children with psoriasis were treated (51:23 female: male). The majority received NB-UVB (n=65) with an average of 20 treatments (range 1-36) and a MCD of 32.10 J/cm2. On completion, 55 children (84.6%) had significantly improved or achieved clearance and 4 children (6.2%) had not improved or worsened. Erythema (grade 2 or above) occurred in 3.4% of all doses for psoriasis, with 30 children (46.2%) developing erythema during their course. Of these: 23 children had grade 2; 6 had grade 3; and 1 had grade 4. One stopped treatment due to grade 3 erythema.

35 patients (53.8%) were discharged after treatment. Relapse occurred in a cumulative total of 17.7% of the children treated by 3 months, 23.8% by 6 months and 28% by 2 years. Of these, 17 required a further course of NB-UVB and one was commenced on acitretin during this follow up period.

Whilst no longer used, we have included data on the use of PUVA and BB-UVB for comparison. PUVA (n=2) resulted in significant improvement in both children treated, with at least 6 months remission. Those treated with BB-UVB (n=7) received an average of 16 treatments (range 12-25) and a MCD of 10.75 J/cm2. Significant improvement or clearance was seen in 6 (86%) and mild improvement in 1 (14%).

*Atopic dermatitis*:

Ten children (7:3 female: male) received NB-UVB with a mean number of 21 treatments (range 1-40) and a MCD of 26.52J/cm2. 7 children had relative topical treatment resistance and 3 underused topical treatments. On completion, 6 (60%) had significantly improved or achieved clearance. These 6 children received a mean number of 30 treatments (26-40). Of the remaining 4 children, all stopped phototherapy within 4 weeks; one had no benefit and the remaining 3 had worsening atopic dermatitis.

Erythema occurred in 2.8% of all doses. A total of 4/10 developed at least grade 2 erythema. One child sustained a grade 3 erythema. No child had to stop treatment because of this. No children stopped treatment due to side effects.

Relapses occurred within 3 months in 4/6 (67%) children who had significantly improved/cleared with treatment. By 2 years, one responder remained controlled on topical treatment alone and 3 non-responders required ciclosporin.

*Vitiligo*:

Eight children (female: male 6:2) were treated for vitiligo with NB-UVB phototherapy. 3 children (37.5%) improved significantly having received an average of 45 treatments (range 20-57), at a mean dose of 29.43 J/cm2 (range 2.99-42.65). Mild improvement was reported in 2 children, who received 131 (47.86J) and 57 treatments (39.56J). Three children did not improve, with an average of 24 treatments (range 14-39), at a mean dose of 7.66 J/cm2 (range 1.32-19.25 J/cm2). Grade 2 or above erythema occurred in only one patient.

Information on relapse rates was not available for this group of children, as they were all either discharged or did not attend for follow up after treatment.

*Other dermatoses*:

A 13-year-old girl with active actinic prurigo was treated with bath PUVA and topical steroids. She received 9 treatments (5.95 J/cm2 total dose) twice weekly at 15% increments, with significant improvement and no subsequent flares over the summer months.

A 10-year-old girl with hydroa vacciniforme received 21 desensitisation treatments of NB-UVB (13.38 J/cm2 total dose). She had an excellent response reporting no blistering over the following summer. After 18 treatments, she experienced grade 3 facial erythema, which settled with topical corticosteroid and an increment reduction from 10% to 5%, for the final 3 treatments.

A 16-year-old girl with PLE received NB-UVB desensitisation. Atypical flaring was reported to have occurred after 5 treatments, hence it was discontinued. A biopsy was consistent with subacute cutaneous lupus erythematosus, although her antibody profile was normal. In view of the histological features of lupus, this case has not been included within the summary table.

NB-UVB was used successfully to treat PLC in 2 children, with 29 treatments (19.94 J/cm2) and 17 treatments (54.37 J/cm2), respectively. The second child relapsed, requiring a second course 9 months later, also with significant improvement. He quickly relapsed again, requiring erythromycin and was lost to follow up. No erythemal episodes were reported in either child.

*Tolerability*

Erythema (grade 2 and above) occurred in 41.9% (36/86) of patients receiving NB-UVB and 2.6% of all treatments. 6 episodes of grade 3 and 1 report of grade 4 erythema occurred over the 17-year period (7/1978 doses; 0.35% of all treatments). Apart from erythema, no other side effects developed in any children over the course of 1517 treatment doses of NB-UVB. In total, 27 children did not complete treatment. This was due to erythema 3 (11%); underlying disease flare 2 (7%); a lack of improvement in 5 children (19%); parental wishes in 5 children (19%) and non-attendance in 12 children (44%).

**Discussion**:

Our retrospective review supports the effectiveness of NB-UVB in the management of childhood psoriasis, where it has the potential to achieve extended periods of remission, as evidenced by our 2-year follow-up period.

In those treated for psoriasis with NB-UVB, significant improvement or clearance was achieved in 84.6% (55/65), with relapse in only 17.7% at 3 months. This contrasts with atopic dermatitis where 60% (6/10) achieved significant improvement but in whom 66% relapsed within 3 months. However, we acknowledge the small sample size of our cohort with atopic dermatitis and our findings should be interpreted with caution. Additionally, most of the children had severe AD with relative topical treatment resistance which may have also contributed to the relative lack of efficacy. Other studies support these findings in childhood psoriasis, but the response of atopic dermatitis is more variable. In a retrospective review of NB-UVB by Pavlovsky et al1 51% (40⁄79) of children with psoriasis achieved clearance and 41% (33⁄79) had a good response. Whereas in those with atopic dermatitis, only 25% (9⁄36) achieved clearance and 44% (16⁄36) had a partial response. Furthermore, psoriasis responders had remission periods of 20 months on average compared with a mean remission of 5 months in atopic dermatitis1. However, longer periods of remission following the treatment of childhood atopic dermatitis with NB-UVB were reported in retrospective reviews by Clayton et al2 (n=50; 50% by 9 months) and Mok et al3 (9/10 at one year).

Whilst our numbers are small there is some evidence both in our review and the literature that NB-UVB may be helpful in the management of vitiligo, AP, HV and PLC in children. Of our 8 patients treated with NB-UVB for vitiligo, 3/8 (38%) obtained significant improvement and 2/8 (25%) mild improvement. A mean of 49 doses (24.84 J/cm2) were given, perhaps suggesting that further treatment may have further improved partial responders. However, it is important to balance these potential benefits with the social impact and potential side effects. Similar response rates were reported for NB-UVB by Percival et al4 in an open uncontrolled study of 28 children with vitiligo. 4/28 (14.3%) had an excellent response and 8/28 (28.6%) a good response. Of 15 children followed up for a mean of 11 months, stable disease continued in 6 (40%) and further improvement was reported in 4 (26.7%).

A retrospective analysis of paediatric phototherapy data in 113 children, by Ersoy-Evans et al5 reported a greater than 75% improvement in 5/5 children with PLC, treated with NB-UVB. A number of other retrospective review support the role of NB-UVB in the treatment of PLC in children.6, 7 In our cohort, NB-UVB led to significant improvement in the 2 children treated with PLC (mean age 14.9 years), however at least one of these children relapsed shortly after completion and the other did not return for follow up, making assessment of sustained benefit difficult.

There is limited data on the use of phototherapy for the management of photodermatoses in children. Over the 14-year period covered by this review, phototherapy was used in the treatment of 3 children with photodermatoses; PLE, HV and AP.

Current treatment options for Hydroa Vacciniforme are limited to photoprotection and photohardening.8,9 The successful treatment of a 10-year-old girl with NBUVB at our centre supports a role for this therapy in the management of this rare photodermatosis.

Phototherapy can be used to treat both active flares of AP and as a desensitisation therapy to prevent future flares. Reports on the use of phototherapy in children with AP are limited. Lee et al10 reported almost complete clearance of lesions and photosensitivity for 4 months in a 10-year-old boy with AP, treated with oral PUVA, 2-3 times/week for 20 weeks. Collins et al9 reported the use of NB-UVB in 3 teenagers with AP, all of which increased their tolerance of sunshine from 30-60 minutes to all day. NB-UVB is considered the phototherapy of choice in AP. Given that the next line therapy in AP is thalidomide, recognition that bath PUVA can be used successfully (as for one child in our cohort) is notable.

Evidence for the use of NB-UVB in the treatment of PLE in children is similarly limited, but the evidence in adults is clear and the treatment is well established.

Long term safety data on the use of NBUVB in children is lacking, but its efficacy, tolerability and safety in children is supported by retrospective reviews.5-7 JAAD guidelines for the treatment of paediatric eczema and psoriasis consider NBUVB to be “safe and well tolerated”.11,12 Furthermore, the same guideline contraindicates PUVA below 10 years of age. Prospective safety data in adults strongly suggests a correlation of squamous cell carcinoma (and to a lesser extent basal cell carcinoma) development with PUVA, especially in those receiving >350 treatments and with higher UVA dosages*.*13 PUVA is no longer routinely used for the treatment of children in our department. Nevertheless, we have included these historical cases in this review for completeness.

41.9% of all patients receiving NB-UVB had at least one grade 2 erythemal episode, with only 0.35% of all treatments resulting in grade 3 or 4 erythema. Whilst these rates appear high, similar rates of erythema are reported in other reviews of childhood phototherapy although with significant variation between studies, ranging from 10-51%.1, 5, 14, 15 Furthermore, a systematic review and meta-analysis of NB-UVB treatment in psoriasis, which was not specific to childhood phototherapy, identified average rates of asymptomatic erythema of 58% and symptomatic erythema of 7.8% of all treatments.16 Nevertheless, at least 3 children stopped treatment as a result of burning. Therefore, clinicians must be aware of the need to provide close counsel during the consent process.

Children “not being brought” for phototherapy was documented as the commonest cause for premature discontinuation of treatment, (44%; 12/27). Thrice weekly NB-UVB can result in significant disruption to schooling, especially when travel time to and from clinic is considered. Where possible, clinicians should try to enable children to undertake phototherapy with minimal disruption to their education. Our department now allocates an hour of phototherapy specifically for children after school, in order to increase attendance.

**Conclusion**:

This review is limited by its retrospective nature, but nonetheless suggests NB-UVB phototherapy should be considered for inflammatory dermatoses before progressing to immunosuppressive treatments in children. This review supports its effectiveness in the management of psoriasis and vitiligo, as well as a number of other rarer dermatoses. Our experience with NB-UVB in the treatment of atopic dermatitis in children is less convincing but should be interpreted with caution given the small patient numbers. NB-UVB is well tolerated in children, but there is a clear need for studies reviewing its long-term side effects.

**References**:

1. Pavlovsky M, Baum S, Shpiro D, Pavlovsky L, Pavlotsky F. Narrow band UVB: Is it effective and safe for paediatric psoriasis and atopic dermatitis? J Eur Acad Dermatology Venereol. 2011;25(6):727–9.

2. Clayton TH, Clark SM, Turner D, Goulden V. The treatment of severe atopic dermatitis in childhood with narrowband ultraviolet B phototherapy. Clin Exp Dermatol. 2007;32(1):28–33.

3. Mok ZR, Koh MJA, Chong WS. Is phototherapy useful in the treatment of atopic dermatitis in Asian Children? A 5-year report from Singapore. Pediatr Dermatol. 2014;31(6):698–702.

4. Percivalle S, Piccinno R, Caccialanza M, Forti S. Narrowband ultraviolet b phototherapy in childhood vitiligo: Evaluation of results in 28 patients. Pediatr Dermatol. 2012;29(2):160–5.

5. Ersoy-Evans S, Altaykan A, Şahin S, Kölemen F. Phototherapy in childhood. Pediatr Dermatol. 2008;25(6):599–605.

6. Pašić A, Čeović R, Lipozenčić J, Husar K, Sušić SM, Skerlev M, et al. Phototherapy in pediatric patients. Pediatr Dermatol. 2003;20(1):71–7.

7. Eustace K, Dolman S, Alsharqi A, Sharpe G, Parslew R. Use of Phototherapy in Children. Pediatr Dermatol. 2017;34(2):150–5.

8. Cohen JI, Manoli I, Dowdell K, Krogmann TA, Tamura D, Radecki P, Bu W, Turk S-P, Liepshutz K, Hornung RL, Fassihi H, Sarkany RP, Bonnycastle LL, Chines PS, Swift AJ, Myers TG, Levoska MA, DiGiovanna JJ, Collins FS, Kraemer KH, Pittaluga S ESJE. Hydroa vacciniforme–like lymphoproliferative disorder: an EBV disease with a low risk of systemic illness in whites. Blood. 2019;133(26):2753–2764.

9. COLLINS P, FERGUSON J. Narrow-band UVB (TL-01) phototherapy: an effective preventative treatment for the photodermatoses. Br J Dermatol. 2010;132(6):956–63.

10. Lee DY, Youn JII, Park MH CJ-H. Actinic prurigo: limited effect of PUVA. Br J Dermatol. 1997;136:972–4.

11. Elmets CA, Lim HW, Stoff B, Connor C, Cordoro KM, Lebwohl M, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with phototherapy. J Am Acad Dermatol [Internet]. 2019;81(3):775–804. Available from: https://doi.org/10.1016/j.jaad.2019.04.042

12. Sidbury R, Davis DM, Cohen DE, Cordoro KM, Berger TG, Bergman JN, et al. Guidelines of care for the management of atopic dermatitis: Section 3. Management and treatment with phototherapy and systemic agents. J Am Acad Dermatol [Internet]. 2014;71(2):327–49. Available from: http://dx.doi.org/10.1016/j.jaad.2014.03.030

13. Stern RS. The risk of squamous cell and basal cell cancer associated with psoralen and ultraviolet A therapy: A 30-year prospective study. J Am Acad Dermatol [Internet]. 2012;66(4):553–62. Available from: http://dx.doi.org/10.1016/j.jaad.2011.04.004

14. Jury CS, McHenry P, Burden AD, Lever R, Bilsland D. Narrowband ultraviolet B (UVB) phototherapy in children. Clin Exp Dermatol. 2006;31(2):196–9.

15. Jain VK, Aggarwal K, Jain K, Bansal A. Narrow-band UV-B phototherapy in childhood psoriasis. Int J Dermatol. 2007;46(3):320–2.

16. Almutawa F, Alnomair N, Wang Y, Hamzavi I LH. Systematic review of UV-based therapy for psoriasis. Am J Clin Derm. 2013;2:87–109.