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Original Article

Comparison of efficacy and safety of topical tacrolimus vs. narrowband ultraviolet B for moderate-severe atopic eczema

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Abstract

Objective To compare the efficacy and safety of topical tacrolimus with narrowband ultraviolet B for moderate-severe atopic eczema.

Methods 60 subjects, equally divided into Group A and B with the former treated with topical tacrolimus and the latter received narrowband ultraviolet B (NB UVB). These patients were followed up at 2, 4, 6, 8 and 12th weeks. Efficacy and side effects of the given treatment were recorded at each visit.

Results 90% of patients receiving NB UVB showed ≥50% SCORAD reduction as compared to 50% of cases applying tacrolimus. Fewer patients (60%) on NB UVB had side effects as compared to 66% of tacrolimus patients.

Conclusion NB UVB is a more effective and safer therapy than topical tacrolimus in moderate-severe atopic dermatitis in our patients.

Key words
Atopic dermatitis; Topical tacrolimus; NB UVB.

Introduction

Atopic dermatitis (AD) or atopic eczema is a chronic dermatological disorder with a variable adult prevalence that ranges from 1.2% in Asia to 17.1% in Europe.[1] AD is diagnosed clinically and presents with papules, vesicles, erythema, excoriations, crusting and lichenification.[2] Atopy is a predisposition to develop sensitization and make Immunoglobulins E when exposed to certain agents, which frequently appears in early life and atopic conditions such as AD, asthma, hay fever, food allergy and allergic rhinitis, very commonly manifest together.[3]

AD has a complex pathogenesis that involves skin barrier abnormalities, genetic predisposition, environmental and immunological factors.[4] AD has the highest disease burden in terms of disability-adjusted life years among all the dermatological disorders and is the 15th most debilitating disease among all the non-lethal conditions.[5] The main burden of AD is due to chronic pruritus, painful skin, poor sleep and low self-confidence.[6]

AD has a chronic course with multiple remissions and relapses and often requires long term management. There are several scoring

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systems used to grade the severity of AD and plan subsequent management such as SCORAD (Scoring Atopic Dermatitis), EASI (Eczema Area and Severity Index), and oSCORAD (objective component of SCORAD).[7] Topical agents like steroids, icthammol, tar and calcineurin inhibitors are used for mild to moderate form of disease. Resistant cases can be treated with systemic therapy which includes corticosteroids, ciclosporin, azathioprine, methotrexate, mycophenolate mofetil, monteleukast, biological agents and intravenous immunoglobulins.[8]

Phototherapy of various types have been proven to be effective for severe AD. The main mode of action of phototherapy in AD is immunosuppression and immunomodulation.[9] NB UVB (wavelength 310-311 nm) is a safe and effective therapeutic modality for several skin disorders including AD. It lowers cytokine production by both Th1 and Th2 lymphocyte cells, proliferation of lymphocytes and natural killer cell activity and improves antimicrobial function of the skin barrier in AD patients.[10]

Tacrolimus is a topical calcineurin inhibitor (TCI) which inhibits T-cell activation and the synthesis of several cytokines.[11] It is a safe and effective therapy in AD and does not cause skin atrophy.[12]

There have been many review articles comparing different AD treatments but no single study has compared NB UVB with topical tacrolimus in these patients. The rationale of our research was to compare the safety and efficacy of these therapeutic options in AD to facilitate clinical decision making in our population.

Methods

Inclusion Criteria Male and female patients aged between 5-60 years presenting with AD diagnosed clinically and having moderate to severe AD based on a SCORAD score >15 were included.[7,13]

Exclusion Criteria Patients on topical AD therapy during last 2 weeks or systemic AD therapy during last 4 weeks, known case of photosensitivity, on photosensitizing therapy, or with known hypersensitivity to tacrolimus were excluded.

Data Collection Sixty participants with AD, diagnosed clinically were included in the study. Their demographic data was obtained and baseline SCORAD score was calculated after informed consent. Patients were divided into two groups. Group A was administered tacrolimus (0.03% for 5-12 years, 0.1% for above 12 years) two times daily over a period of 12 weeks. Group B received NB UVB three times a week over 12 weeks. Emollients were allowed to be used. During treatment patients were observed for efficacy and side effects at 2^{nd}, 4^{th}, 6^{th}, 8^{th}, 10^{th} and 12^{th} week. All the relevant data was documented using a specially designed form.

Efficacy Effectiveness was evaluated by calculating the percentage decrease in SCORAD score, categorized as Poor (<25%), Fair (26-50%), Satisfactory (51-75%), Good (76-90%) and Excellent (91-100%). The therapy was categorized effective when a fifty percent reduction in the SCORAD score compared to the baseline occurred.

Safety The safety of NB UVB was analyzed by monitoring side effects: pigmentation, erythema and burning. The safety of tacrolimus was assessed by observing side effects including burning, pruritus, folliculitis, herpes simplex, or any other skin infection.

Data Analysis The collected data was entered into the SPSS software (version 22) for analysis. Quantitative data were expressed as mean values with standard deviation while qualitative data

were represented using frequency, percentage, and proportions. Chi-square test was applied to see the significance of NB UVB/ Tacrolimus in measuring the efficacy and safety. A p-value ≤0.05 was deemed significant.

Results

The mean age in group A and B was 14.63±9.64 and 24.43±16.21 years respectively. There were sixteen males (53.3%) and fourteen females (46.7%) in group A, while group B had 22 (73.3%) males and 8 (26.7%) females. The therapeutic efficacy of tacrolimus and NB UVB is shown in **Table 1**.

The mean SCORAD score on tacrolimus was 33.96±10.78 at baseline and decreased to 17.06±8.53 at the end of 12 weeks. While that of patients on NB UVB was 44.90±13.53 at baseline and 12.93±8.91 after 12 weeks of therapy. The reduction in SCORAD score was significant in both treatment groups. Furthermore, NB UVB was more efficacious than tacrolimus and this difference was also statistically significant.

Table 1 Efficacy of Tacrolimus vs NB UVB after 12 weeks (n=60).

Efficacy	*Group-A (Tacrolimus) n (%)*	*Group-B (NB UVB) n (%)*
Excellent (91-100%)	1(3.4%)	5(16.6%)
Good (76-90%)	2(6.6%)	11(36.7%)
Satisfactory (51-75%)	12(40%)	11(36.7%)
Fair (26-50%)	15(50%)	3(10%)

Chi-Square= 16.94; p-value = 0.001 (Significant: p-value<0.05).

Table 2 Side Effects of Tacrolimus and NB UVB after 12 weeks (n=60).

Side Effects	*Group-A (Tacrolimus) n (%)*	*Group-B (NB UVB) n (%)*
Skin Burning	15(50%)	3(10%)
Folliculitis	2(6%)	1(3.3%)
Erythema	0(%)	6(20%)
Pruritus	3(10%)	0(0%)
Pigmentation	0(%)	8(27%)

Chi-Square= 0.2871; p-value = 0.591 (Significant: p-value<0.05)

Table 2 displays the side effects seen in both treatment groups. Side effects were statistically insignificant.

Discussion

The treatment of AD is difficult and challenging with many new therapies evolving in the recent past. NB UVB phototherapy and topical tacrolimus are effective time tested treatments of AD.

The male to female ratio in our patients was 2:1.3. Most of the literature reports a higher worldwide prevalence of AD in females for both pediatric and adult populations.[14] Although the epidemiological studies have not been conducted in Pakistan, Saleem *et al*. detected a slight male predominance in children with AD in a recent survey.[15] The observed variation could be due to the relatively small number of patients included in this study.

The mean ages in group A and B were 14 (5-40) and 24 (7-56) years respectively. AD is a childhood disorder as 80% of the patients develop signs and symptoms before the age of 5 years.[2] The reason for this older age range is most likely our exclusion of children below 5 years. NB UVB is avoided in children less than 5 years because of its theoretical long term carcinogenic potential.

In the current study, tacrolimus achieved the targeted improvement in SCORAD (50%) in only half of the patients after 12 weeks of therapy. It was also observed that the maximum improvement in our patients was seen in the initial period of 2-4 weeks. These observations support the fact that tacrolimus is most effective during the initial stages of therapy and the efficacy slows down with continued use. Perala *et al*. from Finland demonstrated efficacy of topical tacrolimus in moderate to severe AD.[16]

Similarly a recent review article by Zhao and colleagues established topical tacrolimus as a safe treatment modality.[17] Another review by Hong *et al*. also supports the use of topical tacrolimus in the treatment of adult AD with efficacy ranging from 36.8% over short term use (12 weeks) to 72.6% over long term use (6 months).[18] Reitamo S *et al*. also observed 65.5% efficacy of tacrolimus in their study with 30% clearance occurring in the initial 2 weeks which is comparable to our study.[19]

More than 90% of the patients in our study showed ≥50% SCORAD reduction with NB UVB, and 63% of the patients showed more than 75% SCORAD reduction in AD. Similarly, Tintle *et al*. documented more than 90% SCORAD reduction with NBUVB therapy over 12 weeks.[20] In our study 40% of the patients with severe AD had more than 75% reduction in SCORAD score. This is comparable to the study by Clayton *et al*. who also observed very good clearance in 40% of their subjects.[21]

The most common side effect with tacrolimus was mild burning sensation (50%) immediately after application which lasted for few minutes and settled after 1-2 weeks. We observed pruritus in 10% of our subjects while only 6% developed folliculitis during therapy. A review by Zhao elicited that burning sensation varied from 0.7% to 47% and pruritus from 2% to 44% in various studies on tacrolimus therapy. The occurrence of folliculitis was usually low (0-14%) which is similar to our results.[17] Burning and pruritus are subjective sensations which probably accounts for the wide difference of their frequency in various studies including ours.

Regarding side effects of NB UVB, 20% of our patients had mild non-tender erythema which settled whereas Tzung *et al*. observed tender erythema in 9% of the patients.[22] UVR compounded with hot humid weather seems to be the reason of increased number of patients having erythema in our study. We observed skin burning in only 10% of our subjects getting NBUVB therapy while none had pruritus similar to the observations of Rossi *et al*.[23]

Limitations The main limitation of the present study was the relatively short duration due to time constraints. Since AD is a chronic disorder safety and efficacy profile of the therapeutic regimens observed over the long term may differ from the observed results.

Conclusion

Both tacrolimus and NB UVB were effective in moderate to severe AD, but NB UVB was more efficacious in severe AD (p=0.041). NB UVB was also found to have better tolerability as compared to topical tacrolimus in terms of incidence of side effects. Future longer duration studies maybe undertaken to support or negate the presented findings in our population.

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