

## COMPARATIVE STUDY OF TOPICAL MOMETASONE FUROATE 0.1%, TOPICAL 0.03% TACROLIMUS, TOPICAL BASIC FIBROBLAST GROWTH FACTOR (bFGF) IN CHILDHOOD VITILIGO

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### ABSTRACT

#### BACKGROUND

Vitiligo, the commonest of all pigmentary disorders, is an idiopathic, acquired cutaneous achromia, characterised by circumscribed, chalky white macules. It may also involve the pigment epithelium of the eyes, the inner ear and the leptomeninges. Although, vitiligo can begin at any age, it develops before the age of 20 years in 50% of the patients and before the age of 10 years in 25% of patients.

#### MATERIALS AND METHODS

The study was conducted for a period of one year with 6 months active intervention. A group of 60 consecutive children attending the outpatient Department of Dermatology were included in this study. The same patients were acting as controls.

#### RESULTS

Grade 4 response was seen in 12 cases (60%) who were on mometasone (VV-20%, focal-30%, segmental-10%), in 10 cases (50%) on tacrolimus (VV-20%, focal-30%) and in 4 cases (20%) on bFGF (focal). Lesions on the face and neck showed grade 4 response in 16 cases (mometasone-8, tacrolimus-6 and bFGF-2), extremities in 6 cases. On the whole grade, 4 response was observed more with mometasone (60%) followed by tacrolimus (50%). Grade 3 response was observed with bFGF (30%).

#### CONCLUSION

Topical mometasone was very effective among the 3 drugs used in childhood vitiligo showing grade 4 repigmentation in all types of vitiligo except mucosal vitiligo. Tacrolimus proved almost as effective as mometasone to restore skin colour in lesions of vitiligo in children. Because it does not produce atrophy or other adverse effects, tacrolimus may be very useful for younger patients, and for sensitive areas of the skin such as eyelids, it should be considered in other skin disorders currently treated with topical steroids for prolonged periods. Topical basic fibroblast growth factor though less effective than mometasone and tacrolimus, but can be tried as initial therapy in resistant cases such as segmental vitiligo as initial therapy of small vitiligo patches when physicians may not like to initiate high risk alternative such as steroids/PUVA as initial therapy in paediatric age where psoralens and steroids should not be initiated because of long-term risks associated with prolonged usage of them as adjunctive therapy to steroids or tacrolimus so as to reduce the dose and duration of steroids or tacrolimus for increasing the overall safety to the child.

#### KEYWORDS

Topical Mometasone Furoate 0.1%, Topical 0.03%, Tacrolimus, Topical Basic Fibroblast Growth Factor, Childhood Vitiligo.

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#### BACKGROUND

Vitiligo, the commonest of all pigmentary disorders, is an idiopathic, acquired cutaneous achromia, characterised by circumscribed, chalky white macules. It may also involve the pigment epithelium of the eyes, the inner ear and the

leptomeninges. Although, vitiligo can begin at any age, it develops before the age of 20 years in 50% of the patients and before the age of 10 years in 25% of patients.

Topical corticosteroids are the main stay of treatment for focal vitiligo, but they are associated with side effects like atrophy and telangiectasia with long-term use. Mometasone furoate belongs to class IV corticosteroids. It has more vasoconstriction property than hydrocortisone, but side effects are similar in both.<sup>1</sup> It has excellent efficacy in the treatment of childhood vitiligo.<sup>2</sup>

Topical tacrolimus is a calcineurin inhibitor. Its use in vitiligo was reported first in 2002.<sup>3</sup> It causes activation of T cells and enhances melanocyte migration and differentiation, which causes repigmentation in vitiligo.<sup>3-5</sup>

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bFGF is a pleomorphic growth factor for various cells including melanocytes. It is secreted by keratinocytes, which causes migration of melanocytes and increases melanogenesis. It acts as a mitogen, chemotactic and chemokinetic agent to melanocytes.

### Aims and Objectives

1. To compare the efficacy of mometasone, tacrolimus and bFGF in childhood vitiligo.
2. To identify the side effects associated with each of them.
3. To analyse the best response among them.

### MATERIALS AND METHODS

The study was conducted for a period of one year with 6 months active intervention. A group of 60 consecutive children attending the Outpatient Department of Dermatology were included in this study. The same patients were acting as controls.

### Inclusion Criteria

1. Clinical diagnosis of vitiligo.
2. Children of either sex, aged below 18 yrs.
3. Has not received any treatment in the past 3 months for vitiligo.

### Exclusion Criteria

1. Age greater than 18 yrs.
2. Noncompliance of the patient (irregular visits, irregular in application of medicine).
3. Patients with rapidly progressing disease.

After obtaining the informed consent, a detailed proforma was filled for each patient covering various aspects like preliminary information (name, age, sex, occupation), history of the present lesions, past history, treatment history, developmental history (for children), family history and personal history (including a history of hobbies causing chemically-induced leucoderma and emotional stress to the patient/child due to the disease).

This was followed by a detailed physical examination, cutaneous examination, examination of mucosae, hair, nails, palms and soles and other systems. The findings were noted in the proforma.

Complete blood picture, ESR, complete urine examination, random blood sugar, blood urea and liver function tests, T3, T4, TSH and stool test were done in all patients. Examination under the Wood's lamp and a skin biopsy were done wherever necessary. Clinical photographs of all the cases and controls were taken.

**Method of Charting the Grid-** An overhead projector transparent sheet was taken with the help of 30 cm scale. Equal squares were drawn measuring 1 square cm each with permanent ink. The lesion on the body of the patient was marked with skin marker. The grid chart was placed on the lesion held static in one portion.

The number of squares occupying the lesion was counted.

Scoring was given in the following manner-

Each full one square cm was- 1.

Any incomplete square was- ½.

Cumulative score = the total number of full squares + (total number of incomplete squares)/2.

Patients were randomly allotted to each group of drugs, firstly, topical mometasone 0.1%; secondly, 0.03% tacrolimus; and thirdly, basic fibroblast growth factor. Patients with flexural or periorbital or active focus of infection falling into topical mometasone were given either topical tacrolimus provided no active focus of infection or else basic fibroblast growth factor, but not mometasone.

The patients on mometasone are advised to apply the cream once daily for 5 days in a week, tacrolimus twice daily and bFGF daily night 2 hrs. before going to bed for 5 days in a week.

Initial size of the lesion was measured with grid chart and gradual improvement in repigmentation was noted by measuring its size in subsequent visits initially once in every 15 days for first 2 months, later monthly once for next 4 months and clinical photographs of all the cases were also taken at each visit. Side effects associated with any of the 3 drugs were also noted.

Grading of repigmentation.

Grade 0- No response.

Grade 1- Minimal <25%.

Grade 2- Moderate <25-50%.

Grade 3- Marked <50-75%.

Grade 4- Excellent <75-100%.

### OBSERVATIONS AND RESULTS

In the present randomised study of 60 children, 20 children were kept on topical mometasone furoate 0.1%, 20 children on topical 0.03% tacrolimus and 20 children on topical Basic Fibroblast Growth Factor (bFGF).

34 (56.66%) children were in the age group 7-12 yrs. and 30% (n=18) of children were <6 yrs. and 13.33%.<sup>6</sup> children were in the age group of 13-18 years. The mean age of the children in the study group was 9 yrs.

The M:F ratio in children was 1:1.31 (Table 1).

The predominant site to be affected in children was face and neck 26 cases (43.33%), followed by extremities, mucosa and trunk.<sup>7</sup>

The disease duration was less than 6 months in 42 patients, 6 months to 1 year in 8 patients, 1 to 2 years in 4 patients and more than 2 years in 6 patients.

A family history of similar lesions was seen in 8 (13.33%) children. History of consanguinity among the parents was seen in 6 (10%) children.

On general examination, clinically detectable anaemia was seen in 8 (13.33%) children and thyroid enlargement was seen in 2 (3.33%) child.

In this study, vitiligo vulgaris is the most common type of vitiligo seen in 24 (40%) children, segmental in 6 patients (10%), focal vitiligo in 18 patients (26.6%) and mucosal vitiligo in 12 patients (20%) (Table 2).

Grade 4 response was seen in 12 cases (60%) who were on mometasone (VV-20%, focal-30%, segmental-10%), in 10 cases (50%) on tacrolimus (VV-20%, focal-30%) and in 4 cases (20%) on bFGF (focal) (Table 3).

Lesions on the face and neck showed grade 4 response in 16 cases (mometasone-8, tacrolimus-6 and bFGF-2), extremities in 6 cases.

In this study, 2 patients developed mometasone-induced acne, 2 patients steroids-induced atrophy on his ankle joint and 4 patients on tacrolimus burning and stinging sensation. No side effects were seen in patient on bFGF.

On the whole grade, 4 response was observed more with mometasone (60%) followed by tacrolimus (50%). Grade 3 response was observed with bFGF (30%) (Table 4).

| Site          | Number of Patients | Percentage |
|---------------|--------------------|------------|
| Face and neck | 26                 | 43.33%     |
| Trunk         | 10                 | 16.66%     |
| Extremities   | 16                 | 26.66%     |
| Mucosal       | 12                 | 20%        |

**Table 1. Site of Vitiligo**

| Repigmentation Score | Mometasone |       |           |         | Tacrolimus |       |           |         | bFGF |       |           |         |
|----------------------|------------|-------|-----------|---------|------------|-------|-----------|---------|------|-------|-----------|---------|
|                      | *VV        | Focal | Segmental | Mucosal | VV         | Focal | Segmental | Mucosal | VV   | Focal | Segmental | Mucosal |
| 0                    |            |       |           |         |            |       |           |         |      |       |           | 2       |
| 1                    |            |       |           | 4       | 4          |       |           | 2       | 2    |       |           | 4       |
| 2                    | 2          |       |           |         |            |       |           |         | 4    |       |           |         |
| 3                    | 2          |       |           |         |            | 2     | 2         |         | 2    |       | 2         |         |
| 4                    | 4          | 6     | 2         |         | 4          | 6     |           |         |      | 4     |           |         |

**Table 2. Effect of Drugs on Different Types of Vitiligo**

\*VV-vitiligo vulgaris.

| Repigmentation Score | Mometasone |               |             | Tacrolimus |               |             | bFGF  |               |             |
|----------------------|------------|---------------|-------------|------------|---------------|-------------|-------|---------------|-------------|
|                      | Trunk      | Face and Neck | Extremities | Trunk      | Face and Neck | Extremities | Trunk | Face and Neck | Extremities |
| 0                    |            |               |             |            |               |             |       |               |             |
| 1                    |            |               |             |            |               |             |       |               | 2           |
| 2                    |            |               |             |            |               | 2           |       | 2             | 2           |
| 3                    |            |               |             | 4          | 8             | 2           | 4     | 4             |             |
| 4                    | 2          | 8             | 4           | 2          | 6             | 2           |       | 2             |             |

**Table 3. Effect of 3 Drugs on Different Sites**

| Repigmentation Score at the End of 6 Months | Percentage of Repigmentation among all Patients Tested |            |      |
|---------------------------------------------|--------------------------------------------------------|------------|------|
|                                             | Mometasone                                             | Tacrolimus | bFGF |
| 4                                           | 60%                                                    | 50%        | 10%  |
| 3                                           | 10%                                                    | 20%        | 30%  |
| 2                                           | 10%                                                    | 20%        | 20%  |
| 1                                           | 20%                                                    | 10%        | 20%  |
| 0                                           |                                                        |            | 20%  |

**Table 4. Results of the Study**

**DISCUSSION**

Childhood vitiligo has been a therapeutic bug bear for several reasons. The two basic aims in the treatment of vitiligo are-

- a) To stop further spread of the disease and
- b) To induce cosmetically satisfying levels of pigmentation (grade 4, i.e. 75-100%) in any give lesion. Topical therapies are essentially indicated when vitiligo affects less than 10% of the body surface area.

The present study is thus an effort to compare and study the efficacy of topical moderately potent steroid 0.1% mometasone furoate, 0.03% tacrolimus and basic fibroblast growth factor in childhood vitiligo.

Out of 60 children, 34 were females and 26 were males. The female-to-male ratio was 1.3:1. The predominance of females is consistent with the results of Halder et al,<sup>8</sup> Narumol Silpa-Archa<sup>6</sup> and Schallreuter et al.<sup>9</sup>

The mean age of onset of vitiligo in the present study was 9 years, which is higher than that found in the study by Halder et al<sup>8</sup> at 4.6 years.

In the present study, the incidence of positive family history of vitiligo is seen in 13.33% (4 cases) of the children. In the study done by Jaisankar et al<sup>7</sup> was 3.3% and Halder et al<sup>7</sup> was 35%.

A history of consanguinity among the parents was positive in 10% (6 cases) of cases. Though comparative

values from other studies are lacking, this may reflect a genetic predisposition to vitiligo.

Hypothyroidism was seen in 33.3% (2 cases) of cases. In the studies done by Grimes et al,<sup>3</sup> 15% has antinuclear antibodies and 15% has thyroid microsomal antibodies.

In the present study, the most common clinical type of vitiligo is vitiligo vulgaris (40%) followed by focal vitiligo (26%), mucosal (20%) and segmental vitiligo (10%). This was similar to studies done by Grimes et al.<sup>3</sup>

In the present study, the most common site is face and neck (43.33%) followed by extremities, mucosa and trunk. This is comparable to the findings of Jaisankar et al<sup>8</sup> where the major site of onset was face and neck (50%), lower extremities (28%), trunk (18%) and perineum (6%). In this study, the predominant skin colour noticed is wheatish (40%), followed by dark (33.33%) and fair (26.66%).

In the present study, the effect of topical mometasone in 20 children showed grade 4 repigmentation on face and neck, extremities, trunk as 40%, 20% and 10%, respectively after 6 months of therapy. Similar study done by Masuria et al. The results are consistent with the studies showing facial vitiligo responding >75% repigmentation than trunk and extremities probably because of higher melanocytic density of facial skin than skin of trunk and limbs. Thus, larger number of residual melanocytes in unaffected fascial skin may further explain the better results of repigmentation of the face.

In the present study, the effect of topical 0.03% tacrolimus in 20 children showed grade 4 repigmentation in 50% of children marked in 20%, moderate in 20% and mild in 10% of children. 4 children had mild burning sensation initially, which subsided in about 2 months.

The effect of topical basic fibroblast growth factor in 20 children showed grade 4 response in 10% cases and grade 3, grade 2 and grade 1 in 30%, 20% and 20% children, respectively. With all the 3 drugs, focal vitiligo responded excellent (75%), predominantly face and neck lesions probably because of higher melanocytic density of facial skin than the skin of trunk and limbs.

## CONCLUSION

Topical mometasone was very effective among the 3 drugs used in childhood vitiligo showing grade 4 repigmentation in all types of vitiligo except mucosal vitiligo. Tacrolimus proved almost as effective as mometasone to restore skin colour in lesions of vitiligo in children. Because, it does not produce

atrophy or other adverse effects, tacrolimus may be very useful for younger patients and for sensitive areas of the skin such as eyelids and it should be considered in other skin disorders currently treated with topical steroids for prolonged periods. Topical basic fibroblast growth factor, though less effective than mometasone and tacrolimus, but can be tried as initial therapy in resistant cases, such as segmental vitiligo as initial therapy of small vitiligo patches when physicians may not like to initiate high-risk alternative, such as steroids/PUVA as initial therapy in paediatric age, where psoralens and steroids should not be initiated because of long-term risks associated with prolonged usage of them as adjunctive therapy to steroids or tacrolimus, so as to reduce the dose and duration of steroids or tacrolimus for increasing the overall safety to the child.

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