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# Comparative Evaluation of Therapeutic Efficacy and Safety of Imiquimod 5% Cream and Tretinoin 0.05% Cream in Molluscum Contagiosum

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**Abstract:** Molluscum contagiosum is a common, benign, viral cutaneous infection. Many treatment options are available including medical and surgical. Though studies have been done to study the effect of topical Imiquimod and Tretinoin in Molluscum contagiosum, not many comparative studies are available between these two drugs. The present study was conducted to compare the efficacy and safety of topical Imiquimod 5% cream and Tretinoin 0.05% cream in Molluscum contagiosum. Total 60 patients were enrolled for the study after taking consent. The 60 patients were divided in to two equal groups of 30 patients. Both the drugs were given to respective group of 30 patients each for home application. Imiquimod was applied every alternate night thrice weekly and Tretinoin was applied every night for eight weeks on the lesions. Both the drugs were kept for 8 hours in night and followed by wash in the morning. Improvement was calculated as grades on the basis of decrease in number of lesions every two weeks for eight weeks up to which the drugs were applied. 43.3% patients of Imiquimod and 30% patients of Tretinoin group had grade 4 (more than 75% of the lesions cleared from the baseline count) improvement. Wilcoxon signed ranks was used for statistical analysis for the efficacy of each drug that resulted in significant p-value which showed that both the drugs are effective and p-value was not significant in both the groups with regard to safety hence both the drugs are safe for the duration used in the study. Comparative evaluation of both the drugs done by Pearson's Chi-square test resulted in p-value (0.079) which was not significant that concludes that both the drugs are equally safe and equally effective in Molluscum contagiosum.
**Keywords:** Imiquimod, Tretinoin, grades of improvement, efficacy, safety.

## INTRODUCTION

Molluscum contagiosum (MC) is a common, benign, cutaneous viral infection caused by the Molluscum contagiosum virus (MCV). Molluscum was described by Bateman in 1817 [1]. These lesions often affect young children, sexually active adults and immune suppressed patients [2]. The lesions are shiny, pearly white, hemispherical, umbilicated papule which may show a central core. The disease is common, with an estimated prevalence of 5–11% [3]. The virus replicates in cytoplasm of all the infected epidermal cells of all the layers. The turnover of cells is increased. The virus does not cross the basal layer. Complete resolution of the lesions can take up to 6 to 8 months, often requiring physical destruction of the lesions. Hence treatment is advocated to hasten the resolution and to limit spread, prevent scarring, secondary bacterial infection, disfiguring and secondary eczematization. Many treatment options are available including medical and surgical. Though studies have been done to study the effect of topical Imiquimod and Tretinoin in Molluscum contagiosum, not many comparative studies are available between these two drugs.

## AIMS AND OBJECTIVES

Comparative evaluation of therapeutic efficacy and safety of Imiquimod 5% cream and Tretinoin 0.05% cream in Molluscum contagiosum.

## MATERIALS AND METHODS

A total of 60 patients of clinically diagnosed Molluscum contagiosum with age 5 to 50 years attending the Department of Dermatology, Venereology and Leprology were enrolled at Guru Gobind Singh Medical College & Hospital, Faridkot after an approval

from the ethical committee. The study included immunocompetent patients with minimum 10 number of lesions, present anywhere on the face, neck, upper limb, lower limb, abdomen and back. Any patient having lesion on genital area and any lesion with inflammation were not included in the study. A brief history with laboratory tests to rule out state of immunosuppression was done.

Patients were divided into two equal groups with 30 patients in each group. Patients of group 1 applied Imiquimod 5% cream over the lesions on alternate night thrice a week and patients of group 2 applied Tretinoin 0.05% cream over the lesions on every night. In both the groups, the applied cream was to be kept for 8 hours in the night followed by wash in the morning. All patients were explained about the procedure in their vernacular language and informed consent was taken. A pre-treatment lesional count with sites involved was documented and photographic record was kept. Patients or parents/guardians (in case of children) were demonstrated the application procedure at the start of study that consisted of cleaning the lesional area with cotton swab soaked in distilled water. It was followed by perilesional application of petroleum jelly with cotton tipped applicator, after which the cream was applied at the centre of the lesion with the base of the toothpick. The procedure was continued till the lesion clears or maximum up to 8 weeks.

Follow up was done after every two weeks till 8 weeks. At every follow up, decrease in number of lesions and any adverse effects were noted. Photographic record was also kept at every visit. Subsequent follow up was done at twelfth and sixteenth week of start of treatment. Only the lesions that were present at start of treatment were evaluated for the response to the treatment.

**Evaluation of the response**

Success of treatment was decided by healing rate of the lesions. Improvement in the lesions was evaluated in the form of grades of response to the treatment as:

Grade 0 = No response = 0 no. of lesions cleared from the baseline count of the lesions.

Grade 1 = ≤ 25% response = less than or equal to one fourth of lesions cleared from the baseline count of the lesions.

Grade 2 = 26-50% response = more than one fourth but less than or equal to half of lesions cleared from the baseline count of the lesions.

Grade 3 = 51-75% response = more than half to three fourth of the lesions cleared from the baseline count of the lesions.

Grade 4 = 76-100% response = more than three fourth to all of the lesions cleared from the baseline count of
the lesions.

Any side effects were also noted.

Recorded results and side effects were analysed photographically and objectively at every follow up visit and compared at end of the study statistically.

**STATISTICAL EVALUATION**

Wilcoxon signed ranks was used for statistical analysis for efficacy and safety of each drug in both the groups individually. Comparative evaluation of both the drugs was done by obtaining p-value using Pearson's Chi-square test. P-value less than 0.05 were considered significant.

**RESULTS**

In the present study, an attempt has been made to compare the therapeutic efficacy and safety of topical Imiquimod 5% cream with topical 0.05% Tretinoin cream in the treatment of Molluscum contagiosum. Maximum number of cases i.e. 53.3% were in the age group of 5 to 10 years. Both the groups were statistically similar with regards to sites of lesion and other demographic data. Most frequent age group in our study consisted of subjects under the age of 10 years with 46.7 % in group 1 and 60 % in group 2. Males outnumbered females in our study making 55% of total cases. Most of the cases in our study were students with 46 cases out of total 60 patients.

After completion of 8 weeks of treatment (Table No. 1), grade 4 improvement was seen in 13 (43.3%) out of 30 patients in group 1 of Imiquimod cream while 9 (30%) out of 30 patients in Tretinoin group showed grade 4 improvement. In both the groups, response was statistically significant. Post treatment follow up of the cases was done at the end of $12^{th}$ and $16^{th}$ weeks. 15 out of 30 patients in Imiquimod group and 11 out of 30 patients in Tretinoin had grade 4 improvements at the end of 16 weeks. Drug application was stopped in the patients who developed complete remission before 8 weeks. Most of the patients in both groups developed erythema and scaling. 3 out of 30 patients in group 1 (Imiquimod) while 5 out of 30 patients in group 2 (Tretinoin) suffered local ulceration. In group 1, 2 out of 30 patients and 5 out of 30 patients in group 2 reported local irritation or pain. No recurrence of old treated lesions was found in both the groups during the study period following the discontinuation of treatment. 4 cases continued to develop new lesions at variable intervals during the course of treatment in both the groups.

**The statistical evaluation showed**

- p-value in intragroup was calculated using Wilcoxon signed ranks, which was significant that shows overall
- The drugs in both Group 1 (Imiquimod 5% cream) and Group 2 (Tretinoin 0.05% cream) are efficacious. When compared, more number of patients had improvement at week 4 and 6 in group 1 as compared to group 2. p-value for the two groups was calculated by Pearson's Chi-square test which was highly significant at 4$^{th}$ week and became significant at 6$^{th}$ week and was not significant at 8$^{th}$ week. This showed that response to treatment with Imiquimod started earlier and was gradual while response to Tretinoin began later but was aggressive. However at 8$^{th}$ week, statistically the p-value was not significant which shows that both the drugs have no difference in the efficacy of the treatment of Molluscum contagiosum with the frequency of application of both the drugs and for the duration which was used in the present study.
- Adverse effects were statistically insignificant in each individual group as evaluated by Wilcoxon signed ranks that shows that both the drugs are safe.
- p-value for adverse effects was statistically not significant which means that both the drugs have comparable safety profile with the frequency of application and duration of both the drugs used in the present study.

**Table-1: Distribution of patients according to improvement at 8 weeks**

| Grade (At 8 week) | | Group | | Total |
|---|---|---|---|---|
| | | 1 | 2 | |
| 0 | Count<br>% within Group | 0<br>0% | 0<br>0% | 0<br>0% |
| 1 | Count<br>% within Group | 0<br>0% | 2<br>6.7% | 2<br>3.3% |
| 2 | Count<br>% within Group | 9<br>30.0% | 4<br>13.3% | 13<br>21.7% |
| 3 | Count<br>% within Group | 8<br>26.7% | 15<br>50.0% | 23<br>38.3% |
| 4 | Count<br>% within Group | 13<br>43.3% | 9<br>30.0% | 22<br>36.7% |
| Total | Count<br>% within Group | 30<br>100.0% | 30<br>100.0% | 60<br>100.0% |

**Table-2: Follow up at 16 weeks**

| Grade (at 16 week) | | Group | | Total |
|---|---|---|---|---|
| | | 1 | 2 | |
| 0 | Count<br>% within Group | 0<br>0% | 0<br>0% | 0<br>0% |
| 1 | Count<br>% within Group | 0<br>0% | 2<br>6.7% | 2<br>3.3% |
| 2 | Count<br>% within Group | 9<br>30.0% | 4<br>13.3% | 13<br>21.7% |
| 3 | Count<br>% within Group | 6<br>20.0% | 13<br>43.3% | 19<br>31.7% |
| 4 | Count<br>% within Group | 15<br>50.0% | 11<br>36.7% | 26<br>43.3% |
| Total | Count<br>% within Group | 30<br>100.0% | 30<br>100.0% | 60<br>100.0% |

At start of treatment with Imiquimod 5% cream

At 4 weeks of treatment with Imiquimod 5% cream

At 16 weeks of treatment with Imiquimod 5% cream

At the start of treatment with Tretinoin 0.05% cream

At 4 weeks of treatment with Tretinoin 0.05% cream

At 8 weeks of treatment with Tretinoin 0.05% cream

**Table-3: Side effects**

| Side Effects | Group1 | | Group2 | |
|---|---|---|---|---|
| | Number | Percentage | Number | Percentage |
| Erythema | 24 | 80% | 27 | 90% |
| Scaling | 22 | 73.3% | 25 | 83.3% |
| Ulceration | 3 | 10% | 5 | 16.7% |
| Irritation/pain | 2 | 6.7% | 5 | 16.7% |
| Any other | Nil | Nil | Nil | Nil |

## DISCUSSION

Multiple treatment modalities are available for Molluscum contagiosum which include mechanical methods like curretage, cryotherapy, evisceration or extirpation, tape stripping, duct tape occlusion etc. These methods are destructive and some are painful, many have irritation as side effect with few having chances of scarring, though minimal. Other treatment modalities at hand are photodynamic therapy, antiviral and immunomodulatory effect based therapies.

Inspite of all modalities, a best method should be effective, painless, cheap, and easily available, should have good compliance for the patient and is without residual scarring.

Imiquimod leads to activation of Toll-like receptor-7 that results in secretion of cytokines primarily interferon-α, interleukin-6 and tumour necrosis factor-α. It also activates Langerhans cells, natural killer cells, macrophages and B-lymphocytes. Imiquimod is well tolerated, the most frequent adverse reaction being local skin reaction with erythema, pruritis, scaling, ulceration and pain. Tretinoin (All-trans-retinoic acid) is a retinoic acid derivative. In addition to immunomodulatory effect, it also has anti-keratinization and antiproliferative action in epidermis thus inhibiting the proliferation of virus [4-6]. It acts by local irritation which damages the viral protein-lipid membrane [7]. Among the side effects, erythema and scaling was most common with both the groups. The scaling and erythema was the desired side effect of our study (Table No. 3). The side effect of ulceration and

pain was not statistically significant. Serious systemic side effects were not observed.

Study by C. Bayer *et al.* for topical efficacy and tolerance of Imiquimod in children suggested that Imiquimod is a useful new treatment in Molluscum contagiosum in children. Imiquimod 1% cream used for MC lesions three times a day, five days a week for four weeks improved lesions though 3 of the 49 experienced a relapse after 10 months and in another study conducted by Rajouria EA, Tretinoin showed good response in Molluscum contagiosum [8].

Molluscum persists in part, because etiological virus produces proteins that antagonise chemokines and impair host cell programmed death (apoptopsis) and interferon is known to induce chemokines and enhance apoptopsis; therefore a local interferon inducer such as imiquimod appears to be reasonable to use in this situation [9]. One study with Tretinoin claimed resolution in 11 days of daily application of Tretinoin [10]. In another study, at the end of 12 weeks, out of 20 patients who received 10% KOH, 17 patients showed complete disappearance, whereas out of 20 patients who received 5% Imiquimod, only 10 patients showed total clearance of the lesions [11]. One study showed topical retinoid is effective treatment of Molluscum contagiosum after six weeks course of treatment as compared with placebo with success rate of 65% and 5% respectively [12]. Retinoids influence proliferation and differentiation of cells and accelerate shedding of corneocytes and as the virus induce hyperplasia so it may be phenomenon behind the resolution of lesion by Tretinoin in regulation of proliferation and shedding of virus containing corneocyte. Also a study of topical retinoids in acne says that initial response to topical Tretinoin may be observd after 2-3 weeks, but substantial clinical improvement can be achieved after 4-6 weeks of continuous therapy, and maximum improvement occurs after 3-4 months, which corresponds to the time taken for response start in our study group of Tretinoin i.e. 6 weeks [4].

Various studies with different duration of application have been done with these drugs in Molluscum contagiosum with many results almost comparable to our study. Topical application of 0.05% Tretinoin cream and 5% Imiquimod cream are two relatively painless, self-applied, home based and hence more compliant modalities for the patient and have been used with success in the treatment of Molluscum contagiosum.

## CONCLUSION

Both the modalities appeared safe and effective with increased compliance of patient as it is home based and self-applied, and as the response increased with time, prolonging the duration of treatment and/or frequency of application of drugs may further improve results. Hence further studies are needed with regard to standardization of duration and frequency of application of the drugs maintaining the safety profile.

To conclude, topical Imiquimod 5% cream and Tretinoin 0.05% cream are the two effective and safe modalities in treatment of Molluscum contagiosum. Though Imiquimod is expensive but the frequency of application required is less. P-value showed that there was no significant difference in the efficacy and safety of the two different modalities.

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