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Original Article

Efficacy and safety of adapalene 0.1 % vs. trichloroacetic acid 30% in management of molluscum contagiosum in children: A randomised controlled trial

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Abstract

Background Molluscum contagiosum is viral infection that is quite common in children. Although many treatment options are available, but these are associated with complications of pain, erythema, scarring or recurrence.

Objective Comparison of efficacy and safety of adapalene 0.1% and trichloroacetic acid 30% in management of molluscum contagiosum in children.

Methods Sample size was sixty. Participants were randomized in two groups. In group A, 30 patients were treated with TCA and in group B, 30 patients were treated with adapalene. Patients were followed for 6 weeks.

Results TCA was found safe in 21 (70%) patients vs. 29 (96.7%) in adapalene group ($p<0.05$). TCA was effective in 25 (83.3%) patients vs. 20 (66.7%) patients in adapalene group ($p>0.05$).

Conclusion It was found that TCA is more efficacious and adapalene is safer.

Key words
Adapalene, trichloroacetic acid, efficacy, safety, molluscum contagiosum.

Introduction

In 1814, molluscum contagiosum was first discovered.[1] and its viral etiology was found by Julisberg in 1906.[2]

It is a DNA poxvirus. It has four types. MCV-1 is the most common and MCV-2 is common in adults and is often sexually transmitted. It is also common in those with immunodeficiency.[3]

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Molluscum contagiosum is a common viral infection of skin in children and most commonly affects school going group. Incidence ranges from 2-8%.[4]

Its incubation period is from 14 days - 6 months. The lesion usually presents as dome shaped, shiny, umbilicated papules. Size varies from 1mm papules to large nodules of 1 cm in diameter. After trauma, inflammatory changes result in crusting, and eventually the lesion is destroyed. New lesions appear due to spread of virus to other areas of skin.[5] The diagnosis of molluscum contagiosum does not pose a problem as it is evident clinically. Although molluscum contagiosum is a self-limiting condition,[6] a study by Vander Wouden JC *et al*.

cites the following reasons for intervention: to relieve discomfort, for aesthetic reasons, social stigma with visible lesion, to prevent its spread and to prevent secondary infection.[7]

There are multiple treatment options for MC. Destructive treatments are cautery, cryotherapy, lesion destruction with needle, electrodessication, and lasers.[8] Chemical destruction with cantharidin is very effective but is associated with blister formation, pain, hypopigmentation or hyperpigmentation,[6] so treatment of facial and diaper region is not recommended with it.[9] Other topical therapies are salicylic acid, tretinoin, KOH, adapalene and TCA (trichloroacetic acid). Imiquimod is topical treatment of choice but causes irritation.[10] Similarly, oral therapy with cimetidine has also been tried; nevertheless, no therapy is universally effective.

Trichloroacetic acid (TCA) is a caustic agent, used in dermatological practice, mostly in the treatment of verrucae.[11] It is safe, low cost and effective agent but erodes skin.[12,13] Cotton-tipped applicator is used for application of TCA till white frost appears, it should be only applied to the centre of lesion.[12] TCA is 90% effective for treatment of molluscum contagiosum.[13] Nevertheless it is irritant and cause pain.

Adapalene is a topical retinoid of third generation mostly used in the treatment of acne, keratosis pilaris and many other skin conditions.[14] Adapalene is not routinely used for MC so no relevant statistics found. But in small concentrations it causes cellular differentiation, keratinization and inflammation. It has both exfoliating and anti-inflammatory effects. In a case report topical adapalene is reported to cause less irritation, low cost and more effective than tretinoin or tazarotene to treat MC.[15] Additionally its application is convenient and easily available in a tube, which might increase the ease of use and compliance.[15] Whereas, TCA needs to be applied by technically trained staff and there is need of repeated outdoor visits of patient. However, no study showing comparison of efficacy and safety of TCA and adapalene is found in literature, so efficacy of adapalene is considered to be 50%.

Rationale of this study is to find topical therapy for MC which is less harmful and more effective.

Methods

This randomized controlled trial was conducted after getting approval from institutional review board, in Department of Dermatology, Lady Reading Hospital Peshawar from March 2021 to September 2021 over a period of 6 months. Data was collected by Systematic randomized sampling technique. Total sample size was 60 (30 in each group). Sample size was calculated by using CPSC recommended formula for two proportions. Power of the test was taken as 80%, level of significance 5%, P1 (for TCA) 90%,[10] and P2 (for adapalene was assumed to be 50% because no study available in previous publications). Children of either gender, age 2-14 years, clinically suggestive of molluscum contagiosum of less than 1 month duration presenting to outpatient department were enrolled in the study. Patients with more than 100 lesions, lesions on eyelids and genitalia and those with history of hypersensitivity to any of test medium were excluded from study. Written informed consent was taken from the patient's parents or guardian. Data was collected on a predesigned proforma. Randomization among the groups was done by lottery method. In group A, thirty patients were treated with TCA 30%. Pointed end of a wooden applicator was used for application of TCA to the centre of lesion till appearance of white frost. Within 1 hour after application of drug immediate adverse effects

(erythema, fever) were noted. Follow up was done on weekly basis and late adverse effects (pigmentary changes, scarring) were noted. Contact number was noted for communication and follow up to reduce lost to follow up cases. Patients were advised to apply adapalene cream 0.1% twice daily in group B for three weeks. Follow-up was done on weekly basis for a total of three weeks. On each follow up visit, lesions were observed for adverse reactions (erythema, crusting, pigmentary changes) and resolution of old lesions. At week 6 the final follow-up was done, three weeks after stopping either treatment to observe if lesions recurred. SPSS version 20 was used for analysis of data. The scale variables were presented as mean±SD. The categorical variables were presented as frequency and percentages. A "p value" of less than 0.05 was considered significant. Effect modifiers like age, no. of lesions, gender and duration of MC were stratified to see the effect of that on outcome by applying chi square test.

Results

There were total sixty patients, 30 in each group.

Mean age in group A was 5.30±3.66 years (range 2–12). Mean age in Group B was 4.37±2.76 years (range 2-14) **(Table 1)**.

There were 20 (66.7%) male patients in Group A and 19 (63.3%) in Group B while there were 10 (33.3%) female patients in Group A and 11 (36.7 %) female patient in Group B **(Figure 1)**.

In both groups lesions were most commonly seen on face **(Table 2)**.

Table 1 Distribution of patients by age (n=60).

Age in years	*Group A No. of patients (%)*	*Group B No. of patients (%)*
2–4	15 (50%)	17 (56.7%)
5–7	7 (23.3%)	8 (26.7%)
8–10	5 (16.7%)	4 (13.3%)
11–14	3 (10%)	1 (3.3)

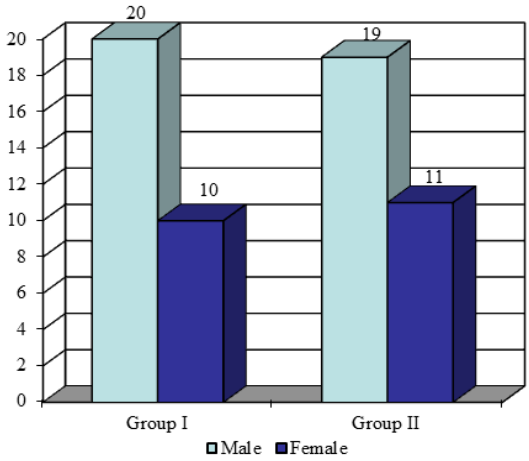

Figure 1 Distribution of patients by gender (n=60).

Table 2 Distribution of the disease (n= 60).

Distribution of the disease	*No. of patients (%)*	
	Group A	*Group B*
Face	11 (36.7%)	13 (43.3%)
Trunk (Front)	6 (20%)	5 (16.7%)
Trunk (back)	5 (16.7%)	4 (13.3%)
Upper Arm	3 (10%)	2 (6.7%)
Lower Arm	1 (3.3%)	2 (6.7%)
Scalp	3 (10%)	2 (6.7%)
Palm and sole	1 (3.3%)	1 (3.3%)
Generalized	0 (0%)	1 (3.3%)

Table 3 Distribution of patients by side effects (n=60).

Side effects	*No. of patients (%)*	
	Group A	*Group B*
Local		
Erythema	3 (10%)	1 (3.3%)
Scarring	1 (3.3%)	0
Hyperpigmentation	1 (3.3%)	0
Hypopigmentation	3 (10%)	0
Crusting	1 (3.3%)	0
Systemic Side effects		
Fever	0	0
Headache	0	0

In group A, erythema was seen in 3 (10%) patients, scarring in 1 (3.3%) patient, hyperpigmentation in 1 (3.3%) patient, hypopigmentation in 3 (10%) patients, and crusting in 1 (3.3%) patient. None of the systemic side effect was seen in this group **(Table 3)**.

In group B, 1 (3.3%) patient developed erythema **(Table 3)**.

Table 4 Distribution of patients by follow up at 6 weeks for disappearance and recurrence of lesions (n= 60).

Follow up at 6 weeks for disappearance and recurrence	*No. of patients (%)*	
	Group A	*Group B*
Disappearance of lesion	25 (83.3%)	20 (66.7%)
Recurrence	5 (16.7%)	10 (33.3%)

Table 5 Distribution of patients by safety (n= 60).

Safety	*No. of patients (%)*	
	Group A	*Group B*
Yes	21 (70%)	29 (96.7%)
No	9 (30%)	1 (3.3%)
P value	0.006*	

* Chi-square test
** Significant

Table 6 Distribution of patients by efficacy (n= 60).

Efficacy	*No. of patients (%)*	
	Group A	*Group B*
Yes	25 (83.3%)	20 (66.7%)
No	5 (16.7%)	10 (33.3%)
P value	0.136	

* Chi-square test
** Not significant

At 6 weeks follow up, in group A, the lesions disappeared in 25 (83.3%) patients and in 20 (66.7%) patients in group B. Recurrence of lesions was observed in 5 (16.7%) patients of group A and in 10 (33.3%) patients of group B **(Table 4)**.

In group A, TCA was found safe in 21 (70%) patients, while in group B, Adapalene was found safe in 29 (96.7%) patients. P-value was 0.006 (significant) **(Table 5)**.

In group A, TCA was found effective in 25 (83.3%) patients, while in group B, Adapalene was found effective in 20 (66.7%) patients. P-value was 0.136 (Not significant) **(Table 6)**.

Discussion

The mean age of the children in both groups was 5.30±3.66 years and 4.37±2.76 years. Rajouria EA *et al.* observed a similar mean age of the patients i.e. 4.3±2.9 years. Mahajan BB *et al.* conducted a study in which he observed mean age of 5.8 years. Similarly, Rajouria and Mahajan also observed that majority of the children were less than 5 years of age.[17,18]

Mahajan B *et al.* conducted a study in India in which majority of patients were male similar to our study. There were 55.6% males and 44.4% females in their study. However, Rajouria conducted a study in Nepal in which majority of patients were female. There were 54.3% females and 45.7% males.

This distribution of lesions in our study was almost same as that described by Rajouria EA, who described that face was affected the most in 41.3% patients.

In our study, the most common adverse reactions with the use of 30% TCA were erythema (10%) and hypopigmentation (10%) due to which it cannot be used on face. However, in a study by Garrette SJ *et al.* TCA was found to be safe and effective. No adverse reactions were observed with 35% TCA among 15 patients over a period of two months. The results of our study contradict with findings of Garrett SJ *et al.* but TCA should be used with caution over face.[16]

Very few complications were seen in our study with the use of adapalene. Erythema was observed only in 3.3% patients. Another study by Gupta R *et al.* also noticed very few complications with adapalene 0.1% for plantar warts. This observation is however contradicted by Inayat S *et al.* who observed a high rate of complications while assessing the tolerability of adapalene in patients with acne vulgaris. Erythema was seen in 13.7% patients and itching was observed in 10.5% patients.[19,20]

In our study, the efficacy of TCA was 83.3%. In

a study by Sadick N *et al.*, TCA was effective in 90% HIV patients with molluscum contagiosum. This study also shows a higher efficacy of TCA, although both studies had different study populations.[13]

No work is done previously to assess the efficacy of adapalene in treating molluscum contagiosum. The results of this study also recommend the use of adapalene although it is not as effective as TCA.

Our study has some. This trial was single centered and sample size was small. As mothers were responsible for applying the topical medication at home so it was not under direct observation. So drug compliance may be an issue.

Conclusion

Although TCA is more efficacious than adapalene for treatment of molluscum contagiosum, but the difference between two is not statistically significant. However, adapalene is safer than TCA. So, adapalene is recommended as first line therapy for treating of molluscum contagiosum. In case of treatment failure, TCA can be used. As adapalene is associated with less complications so it can be used safely over lesions of face.

References

1. Criton S. Viral Infections. Chapter 14 in *IADVL text book and Atlas of Dermatology, 3rd ed*. Valia RG and Valia AR editors, Mumbai: Bhalani Publishing House 2008;333.
2. Sterling JC. Virus Infections. Chapter 33 in *Rook's Textbook of Dermatology. 8th ed*. Burns T, Breathnach S, Cox S, Griffiths C editors, West Sussex, U.K: Blackwell Publishing Ltd., 2010;33:11.
3. Hanson D, Diven DG. Molluscum contagiosum. *Dermatol Online J*. 2003;**9**:2.
4. Gellis SE. Warts and molluscum contagiosum in children. *Pediatr Ann*. 1987;**16**:69-76.
5. Rogers M, Barneson RSC. Diseases of the skin. In: Campbell AGM, McIntosh N *et al*. *Forfar and Arneil's textbook of pediatrics. 5th ed*. New York: Churchill Livingstone 1998;1633-1635.
6. Silverberg NB, Sidbury R, Mancini AJ. Childhood molluscum contagiosum: experience with cantharidin therapy in 300 patients. *J Am Acad Dermatol*. 2000;**43**:503-7.
7. Van der Wouden JC, van der Sande R, van Suijlekom-Smit LWA, Berger M, Butler CC, Koning S. Interventions for cutaneous molluscum contagiosum. *Cochrane Database Syst Rev*. 2009;**4**:CD004767.
8. Metkar A, Pande S, Khopkar U. An open, nonrandomized, comparative study of imiquimod 5% cream versus 10% potassium hydroxide solution in the treatment of molluscum contagiosum. *Indian J Dermatol Venereol Leprol*. 2008;**74**:614-8.
9. Macini AJ, Bodemer C. Viral infections. In: Schachner LA, Hansen RC, editors. *Pediatric Dermatology*. New York: Elsevier 2003;1090-2.
10. Bayerl C, Feller G, Goerdt S. Experience in treating molluscum contagiosum in children with imiquimod 5% cream. *Br J Dermatol*. 2003;**149**:25-9.
11. Scheinfeld N, Lehman DS. An evidence-based review of medical and surgical treatments of genital warts. *Dermatol Online J*. 2006;**12**:5.
12. Bard S, Shiman MI, Betty Bellman B, Connelly EA. Treatment of facial molluscum contagiosum with trichloroacetic acid. *Pediatr Dermatol*. 2009;**26**:425-6.
13. Sadick N, Sorhaindo L. A comparative split-face study of cryosurgery and trichloroacetic acid 100% peels in the treatment of HIV-associated disseminated facial molluscum contagiosum. *Cutis*. 2009;**83**:299-302.
14. Rolewski S. Clinical review: topical retinoids. *Dermatol Nurs*. 2003;**15**:447-50.
15. Scheinfeld N. Treatment of molluscum contagiosum: a brief review and discussion of a case successfully treated with adapalene. *Dermatol Online J*. 2007;**13(3)**:15.
16. Garrett SJ, Robinson JK, Roenigk HH Jr. Trichloroacetic acid peel of molluscum contagiosum in immunocompromised

patients. *J Dermatol Surg Oncol*. 1992;**18**:855-8.
17. Rajouria EA, Amatya A, Karn D. Comparative Study of 5 % Potassium Hydroxide Solution Versus 0.05% Tretinoin Cream for Molluscum Contagiosum in Children. *Kathmandu Univ Med J*. 2011;**36**:291-4.
18. Mahajan B B, Pall A, Gupta R R. Topical 20% KOH-An effective therapeutic modality for moluscum contagiosum in children. *Indian J Dermatol Venereol Leprol.* 2003;**69**:175-7.
19. Gupta R. Plantar warts treated with topical adapalene. *Indian J Dermatol*. 2011;**56**:513-4.
20. Inayat S, Khurshid K, lnayat M, Pal SS. Comparison of efficacy and tolerability of topical 0.1% adapalene gel with 0.05% isotretinoin gel in the treatment of acne vulgaris. *J Pak Assoc Dermatol*. 2012;**22**:240-7.