Original Article
DOI: https://doi.org/10.70749/ijbr.v3i5.1487

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Comparative Study of Cryotherapy Versus 0.05% Tretinoin Cream for the Treatment of Molluscum Contagiosum in Children

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ARTICLE INFO

Keywords: MC-molluscum contagiosum, Cryotherapy, Tretinoin cream.

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Declaration
Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History
Received: 28-02-2025 Revised: 02-05-2025
Accepted: 16-05-2025 Published: 31-05-2025

ABSTRACT

Background: Molluscum contagiosum (MC) is an infection caused by a poxvirus. Although it is a self-limiting condition, active treatment is often necessary to prevent further spread, alleviate symptoms, reduce the risk of scarring, and address cosmetic and social concerns. **Methods:** A randomised controlled trial was conducted at the Pakistan Emirates Military Hospital's Dermatology Department from January to June 2024. It compared the safety and efficacy of cryotherapy versus 0.05% tretinoin in treating molluscum contagiosum. Forty patients were enrolled, with random assignment into two treatment groups. Analysis was performed using IBM-SPSS 21.0, with significance set at $p \leq 0.05$. **Results:** The median age for the cryotherapy group was 7 years (range 3-7), compared to 8 years (range 2-8) in the tretinoin group. The cryotherapy group had a higher proportion of males (60.0%) versus the tretinoin group's 25.0%, while the tretinoin group had more females (75.0%) compared to 40.0% in the cryotherapy group. During the first week, cryotherapy improved lesion counts by 5.8% (from 6.5 ± 3.8), while tretinoin showed a 2.7% improvement (6.8 ± 3.7). Cryotherapy demonstrated superior efficacy over 12 weeks, achieving 100% cure compared to 91.8% with tretinoin. Adverse effects varied, with significant differences in pain, erythema, itching, burning sensation, and erosions. **Conclusion:** Both cryotherapy and 0.05% tretinoin cream were effective and well tolerated. Cryotherapy led to faster resolution of lesions, typically within 12 weeks, and had manageable side effects. Tretinoin cream showed slower lesion resolution but fewer side effects, making it suitable for recurrent cases and children.

INTRODUCTION

Molluscum contagiosum is an infection caused by a poxvirus, specifically the molluscum contagiosum virus (MCV). It is a self-limiting infectious dermatosis that occurs frequently in children, sexually active adults, and individuals with compromised immune systems. The causative agent, MCV, belongs to the Poxviridae family and is primarily transmitted through direct contact with infected skin, which may occur via sexual or non-sexual means, as well as through autoinoculation [1]. The lesions, termed Mollusca, are small, raised, dome-shaped, and typically exhibit a pearly white, pink, or flesh-coloured appearance with a central dimple or pit. They are generally smooth and firm, ranging in size from that of a pinhead to approximately 2 to 5 millimetres in diameter. These lesions may become itchy, sore, red, and/or swollen [2].

Mollusca can appear anywhere on the body, including the face, neck, arms, legs, abdomen, and genital area, either singly or in clusters. However, they are rarely found on the palms of the hands or the soles of the feet [2].

The condition is relatively common, with an estimated prevalence of 5–11%. It is rare in children under the age of one, possibly due to maternally acquired immunity and a prolonged incubation period. In warmer climates, where children are lightly clothed and in close physical contact, household transmission is not uncommon, with the peak incidence reported in children aged between 2 and 5 years. Conversely, in cooler climates, household transmission is infrequent, and infection may occur later, potentially linked to the use of swimming pools and shared bathing facilities. A secondary incidence peak is observed in young adults, primarily due to sexual transmission, with lesions more frequently occurring in the genital region [3].

Treatment approaches that have been employed include caustic destruction using agents such as cantharidin, trichloroacetic acid, and diluted liquefied phenol, as well as irritants like salicylic acid, adapalene, nitric oxide cream, potassium hydroxide, benzoyl peroxide, lemon myrtle oil, and tea tree oil. Surgical methods include cryotherapy and laser therapy, while immunological treatments involve the use of diphencyprone, imiquimod, interferon, cimetidine, intralesional immunotherapy, and surgical excision. All-trans-retinoic acid (tretinoin), readily available in cream form, is believed to work by

inducing local irritation, which disrupts the viral protein-lipid membrane [4].

Although molluscum contagiosum is a self-limiting condition, active treatment may be considered to prevent further spread, alleviate symptoms, prevent scarring, and for cosmetic and social reasons. Current treatment options include physical destruction of the lesions through curettage, cryosurgery, or manual expression, as well as the topical application of caustic agents such as trichloroacetic acid, cantharidin, and silver nitrate [5]. These treatments, however, typically need to be performed in a clinical setting and are often poorly tolerated by children due to the associated pain and fear. Moreover, they can lead to scarring and abscess formation [6]. Topical application of 0.05% tretinoin cream are relatively painless alternatives that have been employed. While 0.05% tretinoin cream is commonly used, its efficacy and safety profiles have varied across studies [7]. In our department, cryotherapy and curettage have conventionally been used for the treatment of children with molluscum contagiosum. However, a non-invasive, painless, and less time-consuming treatment modality was sought. There is also a lack of comparative studies between cryotherapy and tretinoin for this condition. Therefore, this study was conducted to compare the safety and efficacy of these two treatment modalities in managing molluscum contagiosum in children through a randomized controlled trial.

METHODOLOGY

A randomised controlled trial was conducted in the department of Dermatology at Pakistan Emirates Military Hospital. The study spanned six months, from June 2024 to November 2024, and aimed to compare the safety and efficacy of cryotherapy and 0.05% tretinoin in treating molluscum contagiosum. The inclusion criteria encompassed children aged 2 to 12 years, of both sexes, who had been diagnosed with molluscum contagiosum for over a year and had not received any treatment in the preceding three months. Exclusion criteria included patients with immunosuppressive diseases or those who had undergone organ transplantation, as well as patients who had used IFN, IFN inducers, immunomodulators, cytotoxic or immunosuppressive drugs, corticosteroids, or retinoids within four weeks prior to the study's commencement. Patients treated with any topical drug within two weeks before the study or those with dermatological diseases in the treatment area were also excluded.

The study involved the enrolment of 40 patients who met the inclusion criteria. After obtaining informed consent, the patients were randomly assigned to one of two treatment groups, with 20 patients in each group. Group A received cryotherapy using cryospray (liquid nitrogen spray), applied to each lesion for 10–20 seconds in two freeze-thaw cycles, with the procedure repeated after a week if the lesion was not sufficiently cleared. Group B received 0.05% tretinoin cream, applied as a thin film to each lesion daily for up to 12 weeks or until clinical cure was achieved. Patients in both groups were evaluated weekly, with lesion counts, photographs, and assessments of local skin reactions recorded. Efficacy was measured by the complete clearance of all treated lesions, while partial clearance was defined as a 50–99% reduction in baseline lesion count. Safety was assessed by evaluating local skin reactions and adverse events, categorised by severity. The cosmetic outcome was also evaluated based on scarring, atrophy, or pigmentary changes in the treatment area compared to adjacent normal skin. The study's outcome focused on complete clearance with minimal side effects. Statistical analysis was performed using IBM-SPSS 21.0, with descriptive statistics calculated, and chi-square and independent t-tests employed to analyse the data. A significance level of $p \leq 0.05$ was considered statistically significant.

RESULTS

The study involved 40 patients who were evenly divided between the cryotherapy and tretinoin treatment groups, with each group comprising 20 patients. The median age of participants in the cryotherapy group was 7 years (range 3-7), while the median age in the tretinoin group was 8 years (range 2-8), with a p-value of 0.09, indicating no significant difference between the groups in terms of age. In terms of gender distribution, the cryotherapy group had a higher proportion of male patients (60.0%) compared to the tretinoin group (25.0%), while the tretinoin group had a higher proportion of female patients (75.0%) compared to the cryotherapy group (40.0%). The p-value of 0.12 suggests that the difference in gender distribution was not statistically significant as shown in Table 1.

Table 1

Bifurcation of Demographic and Clinical Data with Respect to Treatment Modalities.

Variables	Categories	Treatment modalities		p-value
		Cryotherapy group 20 (50.0%)	Tretinoin group 20 (50.0%)	
Age (years)				0.09
	Median (min-max)	7 (3-7)	8 (2-8)	
Sex				0.12
	Male	12 (60.0)	5 (25.0)	
	Female	8 (40.0)	15 (75.0)	
MC area (mm^2)				0.17
	Median (min-max)	220 (40-550)	220 (55-630)	
Morphology				0.21
	Typical umbilicated papule	1 (5.0)	1 (5.0)	
	Papules exclusively lacking	17 (85.0)	18 (90.0)	
	Umbilication	1 (5.0)	1 (5.0)	
	Atypical presentation	1 (5.0)	-	
Baseline lesion count				0.07
	mean ± SD	7.1 ± 4.1	6.2 ± 3.7	
MC location (%)				0.05
	Face and neck	47	51	
	Trunk	39	41	
	Upper extremity/hands/ genital	24	29	
	Lower extremity	19	21	
	Other	8	5	

SD (standard deviation).

The median area of molluscum contagiosum (MC) lesions was identical in both groups at 220 mm^2, although the range varied slightly more in the tretinoin group (55-630 mm^2) compared to the cryotherapy group (40-550 mm^2). The p-value of 0.17 indicates no significant difference

between the groups regarding lesion area. Regarding the morphology of lesions, the majority of patients in both groups had papules lacking umbilication (85.0% in the cryotherapy group and 90.0% in the tretinoin group), with a small percentage exhibiting typical umbilicated papules (5.0% in each group) and atypical presentations noted in 5.0% of the cryotherapy group only. The p-value of 0.21 suggests that the difference in lesion morphology between the groups was not statistically significant. The mean baseline lesion count was slightly higher in the cryotherapy group (7.1 ± 4.1) compared to the tretinoin group (6.2 ± 3.7), with a p-value of 0.07, indicating no significant difference between the groups in terms of lesion count as shown in Table 1.

The location of MC lesions varied slightly between the groups. In the cryotherapy group, 47% of lesions were located on the face and neck, 39% on the trunk, 24% on the upper extremities, hands, or genital area, and 19% on the lower extremities. In the tretinoin group, 51% of lesions were on the face and neck, 41% on the trunk, 29% on the upper extremities, hands, or genital area, and 21% on the lower extremities. The p-value of 0.05 suggests a borderline significant difference in the distribution of lesions across different body locations between the two treatment groups as shown in Table 1.

During the first week of treatment, the cryotherapy group exhibited a 5.8% improvement in lesion counts, reducing from an average of 6.5 ± 3.8 lesions. In comparison, the tretinoin group showed a slightly lower improvement of 2.7%, with lesion counts averaging 6.8 ± 3.7. By the third week, the cryotherapy group achieved a 37.5% reduction in lesion counts, with the average dropping to 4.9 ± 2.2. Meanwhile, the tretinoin group showed a 32.8% improvement, with lesion counts averaging 5.2 ± 2.4. As the treatment progressed, the cryotherapy group continued to demonstrate superior efficacy. By the sixth week, the lesion counts in the cryotherapy group had decreased by 72.7%, with an average of 2.9 ± 1.5 lesions remaining. In contrast, the tretinoin group showed a 59.5% reduction, with lesion counts at 3.1 ± 1.2. By the ninth week, the cryotherapy group achieved a 92.5% improvement, with lesion counts reducing to 1.3 ± 0.2. The tretinoin group, while also showing significant progress, lagged slightly behind with a 78.1% improvement and an average lesion count of 1.5 ± 0.4. At the conclusion of the 12-week treatment period, the cryotherapy group reached a 100% cure rate, indicating the complete disappearance of all lesions. The tretinoin group, though slightly less effective, still achieved a high cure rate of 91.8%, with the lesion count dropping to an average of 0.3 ± 0.01 as shown in Table 2.

Table 2

Bifurcation of Improvement in Lesion Counts and Complete Cure Rate with respect to Treatment Modalities.

Variables	Treatment modalities			
	Cryotherapy group 20 (50.0%)		Tretinoin group 20 (50.0%)	
Complete cure rate	Lesion counts	% improvement	Lesion counts	% improvement
1-Week	6.5 ± 3.8	5.8%	6.8 ± 3.7	2.7%
3-Week	4.9 ± 2.2	37.5%	5.2 ± 2.4	32.8%
6-Week	2.9 ± 1.5	72.7%	3.1 ± 1.2	59.5%
9-Week	1.3 ± 0.2	92.5%	1.5 ± 0.4	78.1%
12-Week	-	100.0%	0.3 ± 0.01	91.8%

SD (standard deviation).

Pain during application was more frequently reported in the tretinoin group, with 90% of patients experiencing it, compared to 60% in the cryotherapy group, though this difference was not statistically significant (p = 0.22). Erythema, or skin redness, was slightly more common in the cryotherapy group, affecting 45% of patients, compared to 35% in the tretinoin group. However, this difference approached but did not reach statistical significance (p = 0.05). Itching was reported more frequently in the cryotherapy group, with 30% of patients affected, while only 10% of patients in the tretinoin group experienced this side effect, making this difference statistically significant (p = 0.04). The burning sensation was significantly more common in the cryotherapy group, where 90% of patients reported this symptom, compared to 45% in the tretinoin group, a difference that was highly significant (p = 0.001). Erosions, another side effect, were observed in 50% of patients in the cryotherapy group, whereas only 10% of patients in the tretinoin group experienced this, also showing a statistically significant difference (p = 0.001) as shown in Table 3.

Table 3

Bifurcation of Overall Side Effects with Respect to Treatment Modalities.

Variables	Categories	Treatment modalities		p-value
		Cryotherapy group 20 (50.0%)	Tretinoin group 20 (50.0%)	
Pain during application				0.22
	Yes	12 (60.0)	18 (90.0)	
Erythema				0.05
	Yes	9 (45.0)	7 (35.0)	
Itching				0.04
	Yes	6 (30.0)	2 (10.0)	
Burning sensation				0.001
	Yes	18 (90.0)	9 (45.0)	
Erosions				0.001
	Yes	10 (50.0)	2 (10.0)	

DISCUSSION

Molluscum contagiosum virus (MCV) is a large, double-stranded DNA virus belonging to the Poxviridae family, with a global distribution. Unlike other poxviruses, MCV does not establish latency but evades the immune system through the production of virus-specific proteins [8]. Molluscum contagiosum is more prevalent in children but can also affect young adults, in whom it may be sexually transmitted and found in the genital area. In children, the infection is typically not sexually transmitted and is not indicative of sexual abuse. The virus spreads through direct person-to-person contact, autoinoculation, or contact with contaminated objects, such as clothing [9].

Clinically, molluscum contagiosum presents as single or multiple painless white papules with a central depression. These lesions gradually enlarge, reaching a diameter of 5–10 mm over 6–12 weeks. Following trauma or spontaneously after several months, inflammatory changes may occur, leading to pus formation, crusting, and eventual resolution of the lesions. Most cases are self-limiting and resolve within 6–9 months [10].

Despite being benign and generally self-limiting, molluscum contagiosum is often treated by dermatologists

due to the risk of contagion, the potential for surrounding dermatitis, and parental expectations for treatment [11]. Parents are frequently concerned about the social implications for their school-aged children, the continued development of new lesions, and the possibility of spreading the infection to siblings or classmates. Numerous treatment options are available for molluscum contagiosum, broadly categorized into destructive, immunological, and antiviral therapies. Destructive treatments include liquid nitrogen, curettage, and topical preparations such as salicylic acid, potassium hydroxide, and cantharidin, while trans-retinoic acid (tretinoin) may involve the application of tretinoin 5% cream. However, despite the variety of therapeutic options, the treatment of molluscum contagiosum and common warts in children remains unsatisfactory for patients, parents, and physicians alike [12].

Cantharidin is frequently regarded as the treatment of choice in North American literature [13]. It is a vesicant that can induce substantial blistering, potentially leading to pigmentary changes, particularly in individuals with darker skin tones. Furthermore, its availability may be limited in some regions. Curettage, on the other hand, has been shown to be the most effective treatment in terms of the number of visits required and parental satisfaction. However, it must be performed with sufficient anaesthesia to achieve optimal results. Curettage is time-consuming and may not be suitable for a busy clinical environment [14].

Over the past 50 years, considerable experience has been accumulated in the use of cryosurgery for the treatment of skin lesions [15]. Cryosurgery is a widely employed technique for managing molluscum contagiosum (MC). Liquid nitrogen, which has a boiling point of −196°C (−320.8°F), is the most effective cryogen for clinical applications. The mechanism of action involves irreversible damage to the treated tissue due to the formation of intracellular ice. The extent of tissue damage is influenced by the rate of cooling and the lowest temperature achieved. Post-treatment inflammation, which typically develops within 24 hours, further contributes to lesion destruction through immunologically mediated mechanisms [16]. Mild freezing results in dermoepidermal separation, which is particularly effective for treating benign epidermal lesions. Cryotherapy offers several advantages over alternative treatments, including a short preparation time, minimal need for expensive supplies or injectable anaesthesia, a low risk of infection, minimal wound care requirements, and the absence of a need for suture removal [17].

In this study, the demographic and clinical characteristics of patients in the cryotherapy and tretinoin groups were comparable, with no statistically significant differences observed between the groups in terms of age, gender, lesion area, morphology, baseline lesion count, or lesion location. During the initial week of treatment, the cryotherapy group showed a 5.8% reduction in lesion counts, averaging 6.5 ± 3.8 lesions. In contrast, the tretinoin group exhibited a 2.7% improvement, with lesions averaging 6.8 ± 3.7. By the third week, the cryotherapy group achieved a 37.5% reduction, with an average lesion count of 4.9 ± 2.2, while the tretinoin group showed a 32.8% improvement, with lesions averaging 5.2 ± 2.4. By the sixth week, cryotherapy led to a 72.7% reduction, with an average of 2.9 ± 1.5 lesions, compared to a 59.5% reduction in the tretinoin group, which had an average of 3.1 ± 1.2 lesions. At nine weeks, cryotherapy achieved a 92.5% improvement (1.3 ± 0.2 lesions), while tretinoin showed a 78.1% improvement (1.5 ± 0.4 lesions). By twelve weeks, cryotherapy reached a 100% cure rate, with all lesions cleared, whereas the tretinoin group achieved a 91.8% cure rate with lesions averaging 0.3 ± 0.01.

Regarding side effects, pain during application was reported by 90% of patients in the tretinoin group versus 60% in the cryotherapy group, though this difference was not statistically significant ($p = 0.22$). Erythema was slightly more common in the cryotherapy group (45%) compared to the tretinoin group (35%), approaching but not reaching statistical significance ($p = 0.05$). Itching was reported significantly more in the cryotherapy group (30%) compared to the tretinoin group (10%) ($p = 0.04$). A burning sensation was significantly more prevalent in the cryotherapy group (90%) compared to the tretinoin group (45%) ($p = 0.001$). Erosions occurred in 50% of the cryotherapy group versus 10% of the tretinoin group, also showing a significant difference ($p = 0.001$).

In 2011, Rajouria et al. [18] conducted a randomised trial comparing 5% potassium hydroxide (KOH) cream to 0.05% tretinoin cream, both applied nightly. The study involved 50 patients, with 25 assigned to each treatment group. After 4 weeks, a reduction in lesion count was observed in both groups, with the KOH group achieving faster lesion resolution compared to the tretinoin group. However, the tretinoin group experienced fewer side effects, a finding consistent with our own study. Emily Forbet et al. [19] reviewed and updated the management of Molluscum contagiosum, noting retinoids as a potential treatment modality. The overall tolerability of retinoids was reported as excellent, with only two patients experiencing mild irritation, characterised by dryness at the application site. Similarly, in our study, a minimal number of patients reported side effects, primarily a burning sensation.

Limitations

Small sample size and single centre study were limitations of this study.

CONCLUSION

The comparison between cryotherapy and 0.05% tretinoin cream demonstrated that both treatments yielded favourable outcomes and were well tolerated. However, cryotherapy was associated with a more rapid recovery, with the majority of lesions resolving within 12 weeks. Adverse effects with cryotherapy could be minimized when applied according to the specified guidelines. In contrast, 0.05% tretinoin cream exhibited a slightly slower response, with some lesions persisting beyond 12 weeks. Nonetheless, tretinoin cream had fewer side effects and therefore may be preferable for recurrent cases and in paediatric patients.

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