REVIEW ARTICLE

CONTENTS

Molluscum contagiosum: a comprehensive review of treatment modalities

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ABSTRACT

Aim: Molluscum contagiosum (MC) is a common viral skin infection caused by the molluscum contagiosum virus (MCV), a member of the Poxviridae family. Characterized by small, raised, flesh-coloured papules, it primarily affects children but can occur in adults, particularly in immunocompromised individuals. While often self-limiting, the infection can be bothersome due to its contagious nature, potential for spreading and associated discomfort. This article presents a comprehensive review of the current treatment options for MC.

Materials and Methods: A literature search was conducted using PubMed database (2019-2024). The focus was on randomized controlled trials, observational studies, and systematic reviews. After screening 65 abstracts, 43 full-text articles were assessed and 22 were ultimately included.

The therapeutic landscape for MC is diverse, ranging from physical methods and topical agents to immunomodulatory approaches and antiviral drugs. The lack of standardized, universally effective treatment has led to diverse approaches, ranging from benign neglect to aggressive interventions. The choice of treatment is often guided by factors such as the patient's age, the number and location of lesions, the presence of co-morbidities, and the patient's tolerance and preferences.

Conclusions: Given the varied clinical presentation of MC and the absence of a universally accepted standard therapy, several treatment modalities are available, each with its own set of advantages and drawbacks.

KEY WORDS: molluscum contagiosum, molluscum contagiosum virus, poxviridae infections, skin lesions, viral skin diseases

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INTRODUCTION

ETIOLOGY AND CLINICAL PRESENTATION

Molluscum contagiosum (MC) is a widespread viral skin infection caused by the molluscum contagiosum poxvirus (MCV), a member of the Poxviridae family [1]. The visible lesions are often described as pearly, dome-shaped papules with a central umbilication [1, 2]. These papules typically range in size from 1 to 5 mm, although they can sometimes grow to be larger, particularly in immunocompromised individuals [1, 3]. The single or multiple lesions can appear anywhere on the body, but are commonly found on the face, neck, trunk, and extremities [3-5].

EPIDEMIOLOGY

Since the eradication of smallpox, MCV has become the primary poxvirus causing human disease. The global prevalence of MCV infection ranges from 5.0% to 7.5%, with a higher incidence observed in immunosuppressed individuals (5.0–18%) [1]. The transmission of MC occurs through direct skin-to-skin contact, autoinoculation (self-spread), and contact with contaminated objects [6]. While MC predominantly affects children, sexually active adults can also contract the virus [3, 7]. The incidence of MC has been on the rise, associated with sexually transmitted infections and human immunodeficiency virus (HIV) [3, 8]. Moreover, individuals with atopic dermatitis (AD) also exhibit a higher susceptibility to MC, due to skin barrier disruption and impaired immune response [1, 6, 7]. Table 1 summarizes in detail the most common presentation and prognoses of MC by different patients groups.

PATHOPHYSIOLOGY

MCV is a double-stranded DNA virus which specifically infects human epidermal cells, particularly keratinocytes. Following entry into the host, MCV establishes

Tabel 1. Presentation and prognoses of MC by patient group

Characteristics	Immunocompetent pediatric	Immunocompetent adult	Immunocompromised (adult and pediatric)
Age	0–14 years of age most often affected	Typically, young sexually active adults	Might occur at any age
Most frequent locations for lesions	Face, trunk, extremities, axilla	Anus, genital region, lower abdomen, inner thighs	Multiple locations, usually extensive; atypical locations possible
Extent	Limited or diffuse	Often limited to sites of sexual contact	Extensive

Source: based on [8]

Table 2. Available treatment options for

Method	Description	Agents
Physical (surgical)	These approaches directly remove or destroy the lesions and are often considered first-line treatments [11]	Cryotherapy, Curettage, Radiofrequency ablation (RFA)
Chemical	Chemical treatments involve the topical application of substances that destroy infected cells or induce an immune response. Several agents are used, with varying degrees of efficacy and tolerability [11]	Cantharidin, Potassium hydroxide (KOH), Salicylic acid (SA), Glycolic acid (GA)

Source: compiled by the authors of this study

infection in the epidermis and its replication takes place within the cytoplasm of these cells. The viral replication process induces epidermal hyperplasia that may be linked to increased expression of epidermal growth factor receptors (EGFR), stimulating cell division [9]. The rapid proliferation leads to the formation of molluscum bodies, which are masses of viral particles within the cells. These bodies, also known as Henderson-Paterson bodies, are a characteristic feature of MC and can be identified during cytological examination using Tzanck smears. Histopathological examination reveals hyperplastic, endophytic, lobularly arranged keratinized spongy epithelium with eosinophilic inclusion bodies [3, 5, 10]. The virus is thought to utilize the microtubule cytoskeleton within the cell to establish and facilitate the spread of the infection. As the infected keratinocytes differentiate and migrate from the basal layer towards the stratum corneum (the outermost layer of the skin), the mature viral particles are eventually released onto the skin surface, making them available for transmission to new hosts or other areas of the same host. It is crucial to note that MCV does not undergo its complete replication cycle in standard *in vitro* cell cultures. While the virus can enter cells and initiate early gene expression, the subsequent steps of genome replication, virion assembly, and release are not efficiently completed. This makes studying the full replication process and evaluating antiviral drugs challenging. Due to the difficulty in studying MCV replication directly, the vaccinia virus, a related poxvirus, is often used as a model to understand the antiviral properties of potential treatments. The general mechanisms of poxvirus replication are likely conserved between vaccinia and MCV. Their insightful analysis allowed for some early MCV gene identification, which encodes MC160 protein. This protein aids MCV in modulating and evading the host immune response and therefore, it became a target site for novel medications [9].

Despite the fact that MC is often self-limiting, the highly contagious character of the virus and the persistent nature of the lesions can lead to significant discomfort, itching, secondary bacterial infections, molluscum dermatitis, conjunctivitis, and considerable social stigma, which motivates many to seek treatment [2, 10, 11]. The management of MC presents a challenge due to a lack of consensus on the optimal treatment approach. There is no single method universally recognized as superior [1, 11, 12]. The choice of therapy always depends on factors such as the number, location, and size of lesions, the patient's age, immune status, any coexisting conditions such as AD, and the clinician's experience, as well as patient preferences [6].

AIM

This article aimed to provide an in-depth overview of MC treatments, integrating the information from PubMed database. The review covers various approaches to managing MC, with a focus on their effectiveness, safety profiles and suitability for diverse patient populations. By thoroughly analysing and synthesizing the information, it highlights the

complexity of treating MC. It discusses the latest developments in MC treatment, including new topical agents and innovative methods, and offers insights into the challenges and future directions in MC management.

MATERIALS AND METHODS

A comprehensive literature evaluation was conducted between 11.01.2025 – 18.01.2025, using the PubMed database. The search included articles published from January 2019 to December 2024, although in introduction as a source of basic knowledge papers published earlier were used. Key terms included: "molluscum contagiosum", "molluscum contagiosum virus", "poxviridae infections", "skin lesions", "viral skin diseases", and variations of these terms. Looking for appropriate articles, Medical Subject Headings (MeSH) terms were used. The search involved studies published in English, which were also available in full text for free. Titles and abstracts found because of the search were screened for relevance. Full-text articles were then assessed for eligibility. The main goal was to include the newest, most interesting and impactful papers. Selection of the articles was oriented on the texts that provide the broadest view on MC treatment modalities in terms of their mechanisms of action, effectiveness and safety profiles. The primary PubMed search retrieved 123 publications. After screening 65 abstracts, 43 articles were assessed in full text, and 22 fulfilled our inclusion criteria. The literature review considered clinical trials, double-blind randomized controlled trials, meta-analysis, reviews, systematic review articles and case reports. Over 70% of the articles are less than three-years-old.

REVIEW

For the purposes of this review paper, available treatment methods for MC were divided into physical (surgical), chemical, immunomodulatory and antiviral agents (Table 2).

PHYSICAL/SURGICAL METHODS

CRYOTHERAPY

This method uses liquid nitrogen to freeze and destroy the infected tissue. This method is generally effective, with a study showing a clearance rate of 94% [1,12]. However, it can be painful and may cause adverse effects, such as hypopigmentation. Cryotherapy is often performed with a spray gun, applied for 6 to 10 seconds at a 2 cm distance from the lesions [1]. The method requires in-office visits for administration, which can be a challenge for some patients, particularly children. [11].

CURETTAGE

This involves physically scraping off the lesions with a curette and is another effective method, with clearance rates ranging from 70% to 80%. Like cryotherapy, curettage can also cause pain, discomfort, potential scarring, or pigmentary changes. Curettage can be difficult to perform in children due to fear and discomfort [11].

RADIOFREQUENCY ABLATION (RFA)

This procedure uses radiofrequency energy to destroy lesions. While effective, it can be painful, cause crusting, and potentially lead to scarring [2].

CHEMICAL METHODS

CANTHARIDIN

Cantharidin is a naturally occurring compound derived from blister beetles. It is a vesicant that weakens and degrades keratinocyte desmosomes, leading to blister formation and shedding of infected cells [11]. While compounded cantharidin has been used for many years, the recent approval of a standardized drug-device combination product (VP-102) represents a significant advancement [6,11]. VP-102 contains a 0.7% cantharidin solution and is applied using a precision applicator to target individual MC lesions, minimizing the risk of overtreatment and damage to surrounding skin [11]. The CAMP-1 and CAMP-2 trials demonstrated the efficacy and safety of VP-102 in achieving complete clearance of lesions [11,13]. One pooled analysis found a 50% complete clearance rate in the VP-102 group compared with 15% in the vehicle group at day eighty-four [13].

POTASSIUM HYDROXIDE (KOH)

Potassium hydroxide is a caustic agent that destroys infected tissues. Different concentrations of KOH have been used to treat MC, with varying results [7, 11]. A study comparing 10% and 15% KOH formulations showed clearance rates of 58.8% and 64.3%, respectively [11]. KOH can be effective, but it can also cause local irritation, erythema, and burning sensations [5, 14]. One study used 10% KOH solution injected intralesionally. Despite the reported efficacy, some patients experienced significant pain during the treatment [2]. Another study reported 69.40% complete resolution after 12 weeks of topical application of 10% KOH solution.

However, 40% of the participants treated with KOH in this study experienced adverse effects [15].

SALICYLIC ACID (SA)

Salicylic acid is a keratolytic agent that can be used to treat MC. A study compared the use of 30% salicylic acid (SA) solution to 20% glycolic acid (GA) solution. While the complete clearance rate was slightly higher in the SA group (63.33%) compared to the GA group (56.66%), the difference was statistically insignificant. Salicylic acid has shown to have minimal adverse events. Another study showed that 87.5% of patients treated with SA had complete clearance after 24 weeks of treatment. In another study, 30% SA was used and 63.3% of patients had a complete clearance after 4 weeks [7].

GLYCOLIC ACID (GA)

Glycolic acid is an alpha-hydroxy acid that is used as a chemical peeling agent. A study using 20% topical GA in an HIV patient with MC reported the lesions showing responses at week six, with some papules becoming hyperpigmented macules. The side effects of therapy were itching and hyperpigmentation [3]. The same study reported that 20% GA solution was comparable to 30% SA solution [7].

IMMUNOMODULATORY AGENTS

IMIQUIMOD

It is a topical immune response modifier that can be used in the treatment of MC [11,12]. Some study reported complete MC clearance in 92% of cases using a 5% imiquimod cream. However, a Cochrane review found that imiquimod is not better than placebo and may produce adverse effects like pain, blistering, scarring, and pigmentary changes [7,11]. One study reported that using 5% imiquimod cream worsened both MC and AD [16].

ANTIVIRAL AGENTS

BERDAZIMER

This is a first-in-class nitric oxide (NO)-releasing topical treatment, with demonstrated antiviral activity. Berdazimer sodium releases NO when exposed to a proton donor, like water. It has shown to reduce poxvirus replication and inhibit expression of the MCV early gene MC160 [8,9]. Berdazimer gel, 10.3%, has been approved by the FDA as a topical treatment for MC [11, 17]. The treatment is applied as a thin layer to all lesions once daily for 12 weeks [18]. The B-SIMPLE4 trial (phase 3 clinical trial, which included 891 patients) demonstrated a significantly higher complete clearance rate of MC lesions at week twelve in the berdazimer group (32.4%) compared to the vehicle group (19.7%). The study also reported greater reduction of lesion counts in the berdazimer group [11, 18]. In an integrated analysis of the B-SIMPLE 1, 2 and 4 trials, the complete clearance was 30% for berdazimer vs 19.8% for vehicle [19]. In a multi-center study on Japanese patients, more than half of the patients achieved complete clearance by week twelve, with some experiencing complete clearance as early as week 2. Berdazimer gel is a convenient, at-home topical treatment, and does not require application in a healthcare setting [17]. It is generally well tolerated. The most common adverse events associated with berdazimer treatment were application-site pain and erythema, which were mostly mild in severity [13, 18].

CIDOFOVIR

Cidofovir is a nucleotide analogue with antiviral properties that has been used to treat severe and recalcitrant MC lesions, particularly in immunocompromised patients. It is available in both topical and intravenous formulations [12,20]. A study showed that cidofovir 1% cream was an effective therapeutic alternative for MC lesions that are unresponsive to conventional methods in HIV/AIDS patients [12]. However, cidofovir can cause adverse effects, including erosion, inflammation, discomfort, and potential nephrotoxicity with systemic use. The use of cidofovir in treating MC is limited by the difficulty of the virus to proliferate in cell culture [20]. The use of cidofovir requires off-label application because it is not FDA-approved. While it has shown success in some cases, the evidence is anecdotal, and it is not a first-line treatment for MC [12].

THE ROLE OF BENIGN NEGLECT

Many clinicians advocate for a conservative noninterventional approach to MC, also known as "benign neglect" - that is, leaving the MC infection to run its natural course without treatment. MC is typically self-limiting and will eventually resolve spontaneously. Benign neglect might not be suitable for all patients and some people want active treatment (patients with extensive disease, for aesthetic reasons, or in case of secondary complications). It also does not address potential psychological distress or the risk of transmission. A significant percentage of healthcare professionals

recommend benign neglect, but a high percentage of patients, especially parents for their children, desire active treatment [6, 11, 22].

FUTURE DIRECTIONS AND EMERGING THERAPIES

Research into new MC therapies is ongoing. Several promising options have been explored, with varying levels of evidence.

HYDROGEN PEROXIDE (H_2O_2).

It is considered as a treatment option due to its antimicrobial action by oxidation of viral molecules, damaging DNA and causing cytotoxicity. A study has shown that H_2O_2 is a promising therapy due to its safety and low incidence of side effects. However, it is less effective than KOH. It may be a good option for younger children, with more sensitive skin [14].

SPIRULINA

The cream with spirulina, derived from Arthrospira platensis, is another emerging treatment option that shows clinical promise with twice-daily topical applications leading to lesion clearance. A study showed that after 4 months of treatment, complete clearance was achieved in the majority of the patients using this cream. This was a small observational study so at the moment the evidence is limited [21].

RETINOIDS

In severe cases of MC, particularly in immunocompromised patients, oral isotretinoin may be a treatment option. Isotretinoin has shown to be effective in resolving recalcitrant lesions of MC, especially in sensitive areas like the face and neck. It helps with cellular proliferation and differentiation. However, more research is needed to support the use of systemic retinoids for MC, due to the adverse effects associated with their use [10].

DUPILUMAB

Although not a direct treatment for MC, studies have indicated that dupilumab, monoclonal antibody used for the treatment of AD, can lead to the resolution of MC lesions in patients with AD. It has been suggested that the control of AD with dupilumab treatment may help to resolve MC lesions. However, further studies are needed to assess the efficacy of dupilumab in MC [16].

ZINC OXIDE NANOPARTICLES (ZnO-NPs)

ZnO-NPs have demonstrated antiviral activity against the MCV in in vitro studies. They have shown that ZnO-NPs can inhibit MCV replication and reduce viral load. These nanoparticles inhibited MCV replication by more than 75% at a dose of 100 g/mL. ZnO-NPs also decreased the expression of MCV antigens on the surface of BHK-21 cells. Research is still needed to determine the potential for clinical application of ZnO-NPs for MC treatment [20].

MODIFIED AUTOINOCULATION (MAI)

MAI involves intentionally introducing the virus from one lesion into the dermis to stimulate an immune response. Lesions are punctured multiple times using a needle to direct the viral contents into the dermis. One study showed that MAI was more effective than topical KOH. After 16 weeks, 91.48% of patients treated with MAI and 81.64% treated with KOH achieved complete resolution. However, MAI is an invasive procedure and may cause pain and scarring [15].

INTRALESIONAL INJECTION OF ANTIGENS

Another immunomodulatory approach involves the use of intralesional injections of antigens such as cimetidine, interferon alpha, candidine, and diphencyprone, or vaccines like the MMR (measles, mumps, rubella) vaccine [2,4]. These substances are injected directly into the lesion. Some studies have shown promising results, with complete clearance of lesions in 73.3-80% of patients treated with MMR. The most common adverse events were oedema and erythema at the injection site [4].

COMBINATION THERAPIES

Combining multiple treatment approaches may lead to better outcomes. For example, pairing physical treatments with topical medications, and combining antiviral treatments with immunomodulators, can be explored to enhance treatment effects [8, 11].

DISCUSSION

COMPARATIVE ANALYSIS OF TREATMENT METHODS

The efficacy of various MC treatments varies in clinical studies, and there is not a single superior approach [11,12]. Physical methods, such as cryotherapy and curettage, tend to show higher clearance rates, but

Table 3. Common side effects of clinician-applied therapies

Treatment	Side effects	Comments
Cantharidin 0.7% topical solution drug-device combination (device allows for focal application to individual MC lesions)	Vesiculation, erosion, pain, pruritus, erythema, scabbing, discoloration	Approved for patients ≥2 years of age; single application to MC lesions once every 3 weeks (maximum use of 2 applicators per session); allow to dry (should dry within 5 minutes); not required to wash off on the same day (recommended at 24 hours); no occlusion, such as overlying bandages, needed after application; do not apply to mucosal surfaces (e.g., eyes, lips, mouth, vagina); may be used at any skin site affected by MC but not recommended for application within 1cm of any mucosal area, such as eyes, lips (mouth), and vagina.
Cryotherapy	Pain upon and after application, blistering, erythema, edema, crusting, dyschromia (usually hypopigmentation), scarring	Not usually applicable for pediatric patients
Surgery (i.e., curettage)	Pain; need for local anesthesia, scarring, bleeding, secondary infection	Not usually applicable for pediatric patients
Lasers	Pain, dyschromia, postoperative healing	Limited applicability

Source: based on [8]

these methods are invasive, painful, and not well-suited to children who are often most affected by MC (Tab. 3) [11, 19]. Chemical approaches like KOH and cantharidin can be effective, but they can also cause discomfort, irritation, and post-inflammatory changes. Immunomodulators like imiquimod have shown variable results with some adverse effects [7, 11]. Novel therapies like berdazimer gel offer advantages by being self-applied and having a good safety profile [8, 18]. While it may not achieve as high a clearance rate as physical methods, it does offer a good balance of efficacy and tolerability [11, 18]. The development of new, standardized formulations such as cantharidin 0.7% with a precision applicator (VP-102), also helps to address the issues of inconsistent dosing and application [6, 11].

CONSIDERATIONS FOR TREATMENT SELECTION

Selecting the appropriate treatment for MC requires a personalized approach, considering various factors. Firstly, patient age must be taken on board. Children, who are commonly affected by MC, may be less tolerant to painful procedures such as cryotherapy or curettage. Topical treatments such as cantharidin or berdazimer gel may be preferred. The number, size, and location of MC lesions are also critical factors. Lesions near the eyes or genitals need special consideration, and topical treatments may be more suitable. For extensive disease, at home therapies are often preferred [5]. Therapists should always take patient immune status and comorbidities into consideration. Immunocompromised patients may develop severe and recalcitrant lesions that need aggressive treatment, including antiviral therapies such as cidofovir [12]. Patients with AD are more prone to MC. Treatments that are gentle on sensitive skin should be prioritized [1, 16]. In addition, patient preferences and compliance are particularly important. Shared decision-making with patients and their caregivers is essential to determine the most acceptable treatment approach. Clinicians should thoroughly discuss the benefits and risks of each option, as well as the potential for recurrence [6].

LIMITATIONS OF CURRENT RESEARCH

There are several limitations to the research on treatments for MC treatment. Some studies may have small sample sizes, which limit their statistical power. Additionally, many studies use different endpoints, making it difficult to compare outcomes across studies [18]. Some studies use complete lesion clearance as the primary outcome, while others may look at partial clearance, or changes in lesion count [15]. Another issue is that many trials do not track individual lesions, which makes it complicated to assess the effectiveness of a treatment in a particular lesion. Moreover, a lot of studies do not differentiate between new lesions and recurrence of existing lesions [13]. Some studies may not include diverse races and populations, which limits the generalizability of results to other ethnicities. In addition, most trials do not account for long-term outcomes or for the duration of response after treatment cessation. Finally, many studies lack a control group or a placebo arm, making it difficult to determine the true efficacy of a treatment [18]. There is a big need for more robust, large-scale, randomized controlled trials that assess various treatments and combinations of treatments for MC [12, 14].

CONCLUSIONS

Molluscum contagiosum is a common viral infection that presents a therapeutic challenge, with a variety of treatment options available, ranging from physical methods to topical therapies and immunomodulators. A strong patient-physician alliance that includes education about the disease and its treatment is critical to optimizing outcomes. The decision to treat and the choice of method are complex and should be individualized, considering patient and lesion characteristics, clinician expertise, and patient preferences. Given the self-limiting nature of the infection and its tendency to resolve spontaneously, especially in children, a watchful waiting approach may be appropriate in certain cases. Among numerous strategies each have their merits and limitations. Further research is necessary to better understand the efficacy and safety of different treatment modalities. It should address existing restrictions by conducting well-designed, placebo-controlled trials with diverse patient populations and longer follow-up periods. These studies should also explore new drug targets and novel methods to overcome the limitations of current treatments.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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