
Abstract

Background: Molluscum Contagiosum is a common viral skin infection, caused by poxvirus, commonly affects young children. Although there is no specific treatment for this infection, many therapeutic modalities has been used with different success rates.

Objectives: To evaluate the effectiveness of topical 20% KOH, 20% KOH with pricking and pricking alone as comparative treatments for molluscum contagiosum.

Patients and methods: This study was conducted in the Dermatology Clinic of Kufa Medical School Teaching Hospital in Iraq, from August 2011 to January 2013. Ninety patients with Molluscum Contagiosum were recruited. Diagnosis of Molluscum Contagiosum was confirmed on clinical bases. Patients with prior treatment for the last month and patients who had inflamed lesions were excluded. Full history and physical examination were done for all Patients. The patients were divided into three groups: Group 1 included 30 patients treated with topical KOH 20% applied by wooden stick daily at bed time. Group 2 included 30 patients treated by pricking the lesions by 27 G needle wet in 20% KOH weekly. Group 3 included 30 patients treated by pricking alone once weekly.

Treatment sessions were continued until complete cure or maximum of four sessions was achieved. The patients were followed up for two months period from the last session.

Results:

Out of the ninety patients, 57 completed the study. There were thirty one (54.3%) males and 26 (45.6%) females with male to female ratio 1.19-. Their ages ranged from 1.5-62 years (mean and standard deviation of 19.4 ± 16.7). The most common age group affected was below 12 years, 29 (50.8%) patients. The most commonly affected body sites were the face and neck, 49 (85.9%) patients. After 4 sessions, the response rate was as follows:

- Group 1, 17 (94.4%): patients were cured completely and relapse was not recorded; p-value was highly significant (=0.0019).
- Group 2, 20 (86.4%) patients were completely cured and relapse was not recorded; p-value was highly significant (< 0.001).
- Group 3, 12 (75%) patients were completely cured and relapse was not recorded; p-value was highly significant (=0.0014).

Conclusion: Pricking Molluscum Contagiosum by 27G needle alone, pricking with 20% KOH and topically applied 20% KOH all achieved comparable success rates that were all statistically significant. All three methods represented tolerable and highly effective modes of therapy.

Introduction

Part I: Molluscum Contagiosum (MC)

Definition: Molluscum Contagiosum (MC) is a benign viral infection that generally affects young children. It is characterized by smooth, dome-shaped discrete papules that occasionally develop surrounding area of scale and erythema (molluscum dermatitis) [1].

Historical review: MC was first described and later assigned its name by Bateman in the beginning of the Nineteenth Century. In 1841, Henderson and Paterson described the intracytoplasmic inclusion bodies now known as Molluscum or Henderson-Paterson bodies. In the early Twentieth Century, Julinsberg, Wile and Kingery were able to extract filterable virus from lesions and show transmissibility. Goodpasture later described the similarities of Molluscum and vaccinia [2].
**Etiology:** MC is caused by Molluscum virus which belongs to the family Poxviridae subgenus Molluscipox virus, which comprises 4 genetically subdivided but clinically indistinguishable MC viral types [3]. MC virus is a large brick-shaped poxvirus that replicates within the cytoplasm of cells. It shares a number of genomic similarities with other poxviruses, and approximately two-thirds of viral genes are similar to those of vaccinia and variola viruses [4]. MC virus cannot be grown in tissue culture or eggs and although not readily transmissible to laboratory animals, and has recently been shown to produce typical changes on human skin cultured on immunocompetent mice [5]. MC virus type I cause the majority of infection (76%-97%) [6,7]. In patients infected with HIV however, MC virus-2 causes the majority of infection (60%) [8].

There is no relationship between virus type and lesional morphology or anatomical distribution [6,7]. MC virus is passed directly by skin contact to produce the typical cutaneous and, rarely mucosal lesions. Transmission via fomites on bath sponges and bath towels, in beauty parlors, school swimming pools, and Turkish baths have been implicated as a source of infection [9,11].

**Pathogenesis**

The virus replicates within the cytoplasm of epithelial cells, and infected cells replicate at twice the baseline rate. There are many MC viral genes that may contribute to an impaired immune response to this virus, including [12,13]:

1. Homolog of a Major Histocompatibility Class 1 heavy chain, which may interfere with antigen presentation.
2. Chemokines homolog that may inhibit inflammation.
3. Glutathione peroxidase homology that may protect the virus from oxidative damage by peroxidase [12,13].

Infection with MC virus causes hyperplasia and hypertrophy of the epidermis. Free virus cores have been found in all layers of the epidermis. So-called viral factories are located in the Malpighian and granular cell layers. The Molluscum bodies contain large number of maturity virions. These are contained intracellularly in a saclike structure that is thought to alter immunological recognition by the host [12]. Rupture and discharge of the infectious virus –packed cells occur in the center of the lesion. MC virus induces a benign tumor instead of the usual necrotic pox lesion associated with other poxviruses [14].

**Epidemiology**

The virus occurs throughout the world. The disease is common, although the incidence in most areas is not reliably known. Infection follows contact with infected persons or contaminated objects, but the importance of epidermal injury is unknown [15]. It is generally thought to affect human exclusively, but there are a few isolated reports of MC occurring in chickens, sparrows, pigeons, chimpanzees, kangaroos, a dog and a horse [2].

The disease is rare under the age of 1 year, perhaps due to maternally transmitted immunity and a long incubation period [15]. Approximately 80% of the patients are younger than 8 years old, with equal sex distribution [16]. In hot countries where children are lightly dressed and in close contact with one another where personal hygiene may be poor, spread within household is not uncommon [15].

The prevalence of MC virus infection has risen significantly in the past several decades, with an 11-fold increase noted in one US study of patient visits for this disorder over a two decade span. This rise appears to parallel the over all increase in sexually transmitted disease [1]. Although a prevalence rate of less than 5% in US children often cited, the rate varies by location, and it is thought the sub-clinical infection may be more common than overt disease [16].

A representative Australian study documented an overall seropositivity rate of 23%, which supports the view that sub-clinical or mild unrecognized disease exists in the population [17]. A study performed in the Netherlands found the cumulative incidence of the childhood form of MC to be 17% of 15-year old persons [18].

In Iraq, in a study done in 1989 it has been found the incidence of MC among Iraqi children attending dermatology and venerology unit to be 0.2% [19], but nowadays, there is a dramatic increase in the incidence of the infection between Iraqi children (Sharquie personal observation 2008). The prevalence within the HIV population is estimated to be 5-18% and the incidence and severity of MC in acquired immune deficiency syndrome (AIDS) patients is inversely proportionate to the CD4 count [20,21]. In AIDS patients with a CD4 count under 100/ml, the associated incidence of MC is 30% [22].

**Histopathology**

In MC the epidermis is acanthotic. Many epidermal cells contain large, intracytoplasmic inclusion bodies – the so called Molluscum bodies. These bodies first appear as single, minute, ovoid eosinophilic structures in the lower cells of the stratum Malpighii; they increase in size as infected cells move toward the surface. At the level of the granular layer, the staining reaction of Molluscum bodies changes from eosinophilic to basophilic. In the horny layer they measure up to 33 µm in diameter. In the center of the lesion, the stratum corneum ultimately disintegrates, releasing the Molluscum bodies. Thus, a central crater forms. The dermis usually shows little or no inflammatory reaction, except in instances in which the lesion of MC ruptures and discharges Molluscum bodies and horny material into the dermis. Electron microscopic examination reveals that the Molluscum inclusion bodies contain, embedded in a protein matrix, large numbers of MC viruses. They are brick-shaped and measure approximately 300 by 240 nm [23].

**Clinical features**

The incubation period is variously estimated at 14 days to 6 months [15]. MC often presents with extremely small pink, pearly or flesh colored papules, averaging 3-5 mm in diameter, occasionally reaching sizes of up to 3 cm (“giant Molluscum”). As they enlarge, a dome-shaped, opalescent morphology may become apparent. The lesion may have a central dell or umbilication within which a white cured-like substance can be seen that can be expressed with pressure [8,24].

Most patients develop multiple papules, often in intertriginous sites, such as the axillae, popliteal fossae, and groin [1]. Lesions may be grouped in clusters or appear in a linear array. The later often results from koebnerization [24].
Generally, MC can occur on any part of the body surface including face, trunk, extremities, scalp, eyelid, lip, tongue, buccal mucosa, and the soles where the appearance is atypical. MC has occurred in scars in tattoos apparently transmitted in the pigment [15].

Irritated lesions may become crusted and even pustular, simulating secondary bacterial infection. This may precede spontaneous resolution. In addition, in about 10% of lesions, a surrounding eczematous reaction is present (Molluscum dermatitis). Lesions that rupture into the dermis may elicit a marked suppurative inflammatory reaction that resembles an abscess [8]. The duration of both the individual lesion and the attack is very variable and although most cases are self-limiting within 6-9 months, some persist for 3 or 4 years [15].

Three groups are primarily affected: young children, sexually active adults, and immunosuppressed persons, especially those with HIV infection [8]. In young children, the lesions are usually generalized and numbers from a few to more than one hundred. Lesions tend to be on the face, trunk and extremities. Genital lesions occurring as part of a wide distribution occur in 10% of childhood cases. When MC is restricted to the genital area in a child, the possibility of sexual abuse must be considered [8].

In adults, Molluscum can be sexually transmitted and other STDs may coexist. There are usually fewer than 20 lesions; these favor the lower abdomen including the pubic area, upper thigh, and the penile shaft in men. Mucosal involvement is very uncommon. Immunosuppression, either systemic T-cell immuno-suppression (usually HIV, but also sarcoidosis and malignancies) or abnormal cutaneous immunity (as in atopic dermatitis or topical steroid use), predispose the individual to infection. In atopic dermatitis, lesions tend to be confined to dermatitic skin [8].

Recent studies have suggested that molluscum contagiosum may serve as a cutaneous marker of severe immunodeficiency and sometimes is the first indication of HIV infection [25]. Ten to 30% of AIDS - patients not receiving antiretroviral therapy have MC. In untreated HIV disease, lesions favor the face (especially the cheek, neck, and eyelids) and genitalia. They may be few or numerous, forming confluent plaques. Giant lesions are not uncommon. Involvement of the oral and genital mucosa may occur, virtually always indicative of advanced AIDS (helper T-cell count <50). Facial disfigurement with numerous lesions can occur [8].

Diagnosis

It is easily established in most instances because of distinctive central umbilication of the dome-shaped lesion. This may be enhanced by light cryotherapy that leaves the umbilication appearing clear against a white (frozen) background. For confirmation, express the pasty core of a lesion, squash it between two microscopic slides (or a slide and a cover glass) and stain it with Wright, Giemsa, or Gram stain. Firm compression between the slides is required [8]. Histopathological evaluation can be performed as needed [1].

Diagnosis can be carried out rapidly by electron microscopy [15]. A quick and reliable in-clinic method to confirm the diagnosis of MC using 10% KOH solution which is added to crushed material of the core of MC, keratin will sufficiently clear within minutes, and the clustered, round or oval shaped Henderson Paterson bodies are easily seen within the specimen[26].

Molecular analysis of DNA from specimens confirms MC using hybridization or PCR techniques [27,28]. Detection of serum antibodies to MC can be measured by several techniques including complement fixation, tissue culture neutralization, fluorescent antibody, and gel agar diffusion. However, they are neither appropriate nor readily available for routine diagnosis [29,30,32].

Complications and associated symptoms [1,15]

1. Pruritus, particularly in those patients with underlying atopic dermatitis.
2. Secondary bacterial infection can occur, particularly if patients scratch their lesions.
3. Chronic conjunctivitis and punctuate keratitis may develop in patients with eyelid lesions.
4. Erythema annulare centrifugum has been reported.

Prevention: [1,8]

1. Avoid trauma to the sites of involvement.
2. Avoid scratching.
3. Autoinoculation may be decreased by treating all existing lesions.
4. Shaving with blade razor should be discontinued if MC affects the beard or any hairy areas.
5. Avoid contact sports, sharing towels and swimming baths.
6. Avoidance of multiple sexual partners.

Treatment

In many instances, complicated therapy is not necessary and natural resolution can be awaited. This generally occurs without complications but often over a prolonged period of months to years in immunocompetent individuals. When lesions are symptomatic or associated eczema is troublesome, treatment may be desirable. The choice of treatment will depend on the age of the patient and number and position of the lesions [1,15].

Type of treatments is arranged according to immune status of patients

Immunocompetent individuals:

Surgical treatment:

Curettage: Recently, curettage was found to be more efficient and had a lower rate of side effects than other therapeutic options. However, curettage may be associated with scarring and is not well tolerated by children if performed repeatedly, owing to pain and fear. The lesions are scraped away with a Hebra curette on day zero and on day twenty-eight if necessary. A local anesthetic (EMLA cream) is applied under occlusion prior to the procedure to decrease the pain. Patients and parents are advised on local care of the treated areas with

povidone-iodine. Sixty-six percent may not be cured after one session. The proportion of patients that may be cured after two sessions of curettage remain high (45%). Risk factors for relapse are the number of lesions at day zero, more than 80% of patients with more than 10 lesions presented with MC relapse, 1 month after the first session of curettage. Other risk factors for relapse are the number of involved anatomical sites, the presence of concomitant atopic dermatitis and the size of the largest lesion [33].

Evisceration: An easy method to remove the lesions is eviscerating the core with an instrument such as a scalpel, sharp tooth pick, edge of glass slide, or any other instrument capable of removing the umbilicated core. This method may not be tolerated by small children [34,35].

Cryosurgery: It is one of the most common, quick, efficient methods of treatment. Liquid nitrogen or dry ice are applied to each individual lesion for a few seconds, repeated treatments in 2-3 week interval may be required. Hyper- or hypopigmentation and scarring may be caused by this treatment [36].

Topical treatment

Cantharidin: Cantharidin 0.7% or 0.9% liquid, is extract of the blister beetle, cantharis vesicatoria, induce vesiculation at the dermoepidermal junction when applied topically to the skin. It must be applied with care and washed off 2 to 6 hours later. Use on the face or genital areas is not recommended. Cantharidin can induce severe blistering. It should be tested on individual lesions before use on large numbers of lesions. When tolerated, the treatment is repeated every week until the lesions clear. Usually, 1-3 treatments are necessary. It leads to resolution in 90% of patients and 8% of patients improved. This therapy has a very high satisfaction rate for patients and their parents, and has rare complications (severe blistering & scarring) [37].

Podophyllin and podophyllotoxin: Podophyllin is a plant compound that causes cells to arrest in mitosis, leading to tissue necrosis. Podophyllin resin 10% to 25% in compound tincture of benzoin used to be the standard provider-administered therapy [38].

It is used once weekly by cotton tipped applicator. The treatment requires some precautions. It contains two mutagens, quercetin and kaempferol. The side effects include severe erosive damage in adjacent normal skin that may cause scarring and systemic effects. Podophyllotoxin is a safer alternative and may be used by patients at home. The recommended use usually consists of application of 0.05 ml of 5% podophyllotoxin in lactate buffered of ethanol twice a day for 3 days per week. They are absolutely contraindicated in pregnancy [39].

Imiquimod: A topical immune response modifier that produce a localized immune response at the site of application, stimulate the monocyte/macrophage and dendritic cells to produce interferon alfa (IFN-α), several interleukins, and tumor necrosis factor (TNF), all leading to cytotoxic T-cell activity [40]. Imiquimod also stimulates migration of Langerhans cells to lymph nodes enhancing virus-specific T-cell production [41]. Imiquimod 5% cream used to treat MC by daily application for 8-12 weeks with clearance of 75%-82% of patients [42]. This potent immunomodulatory agent is well tolerated, although application site irritation is common. It has had no known systemic or toxic effects in children [43].

Iodine solution and salicylic acid plaster: A 10% iodine solution is placed on the molluscum papules and, when dry, the site is covered with small pieces of 50% salicylic acid plaster and tape. The process is repeated daily after bathing. After lesions have become erythematous in 3-7 days, only the iodine solution is applied. Resolution has been reported in mean of 26 days. Maceration and erosion can result [44,45].

Tape stripping: Continuous application of surgical tape to each lesion daily after bathing for 16 weeks led to cure in 90% of children so treated. The tape was cut to the size of each lesion. It was reapplied after each bath or if it fell off. After 3 weeks of therapy, most of the lesions were crusted over. This treatment was well tolerated, with no pain or irritation. This treatment modality had several advantages that are non-destructive, painless, home applied, and cheap [46].

Tretinoin: Successful therapy with topical tretinoin cream has been described in MC. Twice daily application of 0.1% tretinoin leads to resolution of lesions after 11 days of therapy. Tretinoin 0.05% cream used, a similar result was obtained. The mechanism of action of tretinoin may relate to its ability to produce marked inflammatory reaction of the skin that may be important as a local defense against the virus. Good results with the highest tolerated concentration of tretinoin applied nightly have also been reported to reduce the size and frequency of new lesions. Skin irritation characterized by erythema, peeling, dryness and pruritus have been reported as a possible side effects [46].

Nitric oxide cream: Topical 5% sodium nitrate with 5% salicylic acid applied to each individual lesion every night under occlusion, the cure rate was about 75%. Nitric oxide has specific antiviral effects at levels below those toxic to host cells, by inhibiting viral replication. It probably acts on several targets by inhibiting RNA synthesis, DNA replication, and early and late viral protein synthesis and by nitrosylating viral structural proteins. Nitric oxide causes lymphocyte, macrophage and neutrophil infiltration, expression of adhesion molecules and migration of antigen-presenting cells. Also there is an increase in p53. It is therefore, possible that nitric oxide acts through DNA toxicity to infected cells, promoting apoptotic cell death. Staining of skin and irritation were frequent side effects [47].

Silver nitrate paste: Silver nitrate paste 40% used effectively in the treatment of molluscum contagiosum, the cure rate was 97.7% and no scar resulted. The paste applied to the MC with a blunt-ended or pointed toothpick. The lesions to be treated are first prepared with 2% lidocaine jelly, which not only diminishes pruritus or pain but prevent an erythematous flare after application of the paste. Within 1 day, black crusts form over the treated MCs. Ten to 14 days after the application, MCs drop off the skin as black dry crust, and within 1 month the treated lesions heal without leaving scars [48].

Immunotherapy: The treatment consists of intranasal injection with Candida Albicans skin test antigen for cellular hypersensitivity. A total of 0.3 ml was injected into either one lesion or divided between two lesions at monthly intervals. Average numbers of injections are
2-4. The injected killed yeast protein will not only mount an immune response locally to the yeast protein but also against the Molluscum virus. This stimulated immune response could then subsequently destroy all lesions on the body, rather than locally treating each lesion. Sixty-five percent had complete resolution, 28% had partial clearing, and 16% had no improvement. No serious side effects were reported apart from discomfort, erythema, post inflammatory hyperpigmentation, bulla and crusting [49].

Lactic acid: Lactic acid works as an exfoliant, reduce the thickness of stratum corneum by reducing corneocyte cohesion, so it causes the cells of the epidermis to become “unglued” allowing a dead skin cells to slough off making room for regrowth of the new skin It may even stimulate the production of collagen and elastin by fibroblast and it may increase production of ground substance, also it acts as humectants, therefore, lactic acid used in dermatology for treatment of M.C., warts, xerosis of the skin, ichthyosis, follicular hyperkeratosis and seborrheic keratosis [50,54].

Potassium hydroxide (KOH): KOH solution is used in different concentrations such as 5%, 10% and 20%.

Systemic treatment

Oral cimetidine: Cimetidine is a histamine 2-receptor antagonist classically administrated to suppress gastric acid secretion and treat peptic ulcer disease. It also has immunomodulatory effects by stimulating delayed-type hypersensitivity. The T suppressor lymphocytes are known to possess histamine receptors. Cell-mediated immunity is believed to be enhanced by cimetidine by preventing histamine-induced stimulation of T suppressor activity. It has been used in varicella zoster and herpes simplex, chronic mucocutaneous candidiasis, multiple viral warts and verruca plana, urticaria and others. Cimetidine 40 mg/kg/day were prescribed in two to three divided doses either as tablets or liquid suspension. The standard treatment period was two months. The cure rate was about 69% during this period. The side effects are infrequent and include nausea, diarrhea, skin rash, and dizziness. Drug interactions occur with phenytoin, warfarin, propranolol, theophylline and others [56].

Molluscum Contagiosum in HIV-positive patients: MC in HIV-positive patients is notoriously difficult to treat [57], and unlike otherwise healthy hosts, there is no evidence that lesions spontaneously resolve [58]. Perhaps the most widely used methods are curettage and cryosurgery. Tretinoin may serve as a helpful adjunct to any locally destructive therapy through daily application [59].

Some researchers have reported success in AIDS patients by using nightly tretinoin as an adjunct to cantharidin (applied for up to 24 hours) on body and facial lesions followed by curettage for recalcitrant lesions [60]. Intramuscular and systemic interferon have been used with minimal to moderate success in treating AIDS patients with MC [61,62]. Imiquimod has been studied in AIDS and certainly deserves consideration as a potential therapy [63]. Crude podophyllin extract might be a poor choice in an HIV infected patient, given the predisposition for the development of cancer in these patients [64].

At least 3 case reports describe the reduction in number of patients’ extensive mollusca after beginning potent combination antiretroviral treatment [65,67]. In one early case, a patient improved after initiation of zidovudine [65], and in more recent case, a patient improved after starting retinoavir [66].

This highlights an important point: every attempt should be made to optimize treatment of the HIV infection in patients affected with MC because this will make treatment of the MC infection more feasible [58].

Other modalities used in AIDS-associated MC include the following:

Trichloroacetic acid peel: Trichloroacetic acid peel was used in the treatment of human immunodeficiency virus patients with extensive facial MC. Peels were performed with 35 to 50% trichloroacetic acid (average 35%) and were repeated every 2 weeks as needed. A total 15 peels were performed with an average reduction in lesion counts of 40.5% (range 0 to 90%). No spread of Molluscum lesions, scarring, or secondary infection developed at 2 months follow up. Trichloroacetic acid peeling in concentration of 35% or less appears to be safe, effective, adjuvant therapy in the treatment of extensive MC in immunocompromised patients [68].

Potassium hydroxide (KOH): KOH solution is used in different concentrations such as 5%, 10% and 20%.

Cidofovir: Cidofovir is a nucleoside analogue of deoxyxytidine monophosphate that has antiviral activity against a broad range of DNA viruses. The active metabolite, cidofovir diphasophate bears structural similarity to nucleotide and acts as a competitive inhibitor and an alternative substrate for DNA polymerase. Topical cidofovir 1% or 3% cream or solution used successfully in the treatment of AIDS related extensive molluscum contagiosum, it is used 5 times / week for 8 weeks [69,71].

Electron-beam therapy: [72] The use of electron beam energy in the treatment of cutaneous MC lesions in patients with AIDS suggests a potential and promising role for radiation therapy in these individuals. It has been used in AIDS-related recurrent MC lesions at one or more body sites. Treatment was administered by using mega electron voltage (9 MeV or 12 MeV) electron-beam energy. The selection of the radiation technique was determined on the basis of the location and size of the lesion site. Treatment administered five times per week for up to 18 treatments per site, with duration dependant on the severity of the lesions unless an acute toxic reaction to irradiation developed. Response assessed clinically. Patient who had complete resolution of the symptoms or disappearance of the MC lesions at examination were considered to have had a complete response. Those with substantial but incomplete reduction of the lesions (i.e. greater than 50% decrease in size) were considered to have had a partial response. Lesions that were minimally affected by the treatment were considered not to have responded. At least partial regression of most lesions occurred after the 1st week of treatment. Some patients needed 10 treatments for complete resolution and other patients needed 18 treatments. Mild skin erythema was reported in some patients. No
lesion recurrence has been noted during the follow up period (range 14-24 months).

**Introduction**

**PART II: Potassium hydroxide (KOH)**

**Pharmacopeia description:**

Chemical name: potassium hydroxide.

Other names: caustic potash, potash lye, potassa, potassium hydrate and lye [73].

Molecular formula: KOH [74].

It is a white, crystalline, hard mass, supplied as sticks, pellet, or irregularly shaped pieces, it is deliquescent in air, hygroscopic, and absorbs carbon dioxide. It is very soluble in water, freshly soluble in alcohol and in glycerin; very soluble in boiling alcohol. It is stored in air tight, non-metallic containers [74,75].

It contains not less than 85% of total alkali, calculated as KOH, including not more than 3.5% of anhydrous potassium carbonate. Exposed to air, it rapidly absorbs carbon dioxide and moisture, and deliquesces. Soluble 1 in 1 of water, 1 in 3 of alcohol, and 1 in 2.5 of glycerol [74,75].

Potassium hydroxide is obtained commercially from the electrolysis of potassium chloride solution in the presence of a porous diaphragm. The reaction can be characterized as follows:

\[ \text{KCl} + \text{H}_2\text{O} \rightarrow \text{HCl} + \text{KOH} \]

Generally, KOH is considered a by-product of hydrochloric acid and chlorine manufacturing [73].

Potassium hydroxide is a strong base and is alkaline in solution. It is highly corrosive. Caustic peeling is based on the differential solubilization of the cell and tissue constituents [76]. Potassium hydroxide solution is a strong alkali that penetrates deeply and destroys the skin because it dissolves keratin. It can also cause an irritant reaction in the skin varying with concentration, body region and individual susceptibility [77].

**Uses**

1. Its main uses in food processing include use as a direct additive, formulation aid, and pH adjuster, cleaning agent, stabilizer, thickener and poultry scald agent. It is used in dairy products, baked goods, cocoa, fruits, vegetables, soft drinks, and poultry.
2. Non-food uses include: soap manufacture; electroplating printing, as a mordant for wood; as a highly reactive source of potassium in a wide variety of industrial chemical syntheses and chemical analyses; in veterinary medicine as a caustic used in disbudding calves horns and in aqueous solution to dissolve scales and hair in skin scrapings, manufacture of cleansers.
3. Uses in dermatology:

   **diagnostic:** potassium hydroxide solution 10-20% used for diagnosis of superficial fungal infection such as dermatophytopses, onychomycosis, tinea nigra, piedra and also used for diagnosis of yeast infections such as candidiasis and tinea (pityriasis) versicolor. Scales or plucked hairs can be dissolved in an aqueous solution of 10-20% (KOH). Potassium hydroxide dissolves material that binds together cells but does not distort the epithelial cells or fungi [78].

**Therapeutic**

1. Potassium hydroxide is a powerful caustic which has been used to remove warts [75].
2. Treatment of genital warts in men with KOH 5% aqueous solution [79].
3. Treatment of MC with 5%, 10% and 20% KOH solution [80,83].

**Adverse effects:** Potassium hydroxide is a strong alkaline agent. It causes injury to tissue by liquefaction necrosis. It can be rapidly progressive and results in extensive penetrating tissue damage. Saponification of fats and solubilization of proteins allow deep penetration into tissues. It can also cause an irritant reaction in the skin, symptoms of irritation include redness, burning and itching [60].

**Aim of the study**

Is to evaluate the effectiveness of topical 20% KOH, 20% KOH with pricking and pricking alone in treatments of molluscum contagiosum.

**Patients and Methods**

This therapeutic single blinded comparative study, was conducted in the Department of Dermatology and Venereology, Kufa Medical School teaching hospital, Najaf, Iraq.

A total number of ninety patients with MC were enrolled in this study. All patients were diagnosed on clinical basis. Patients with prior treatment in the last 4 weeks, patients with inflamed lesions and pregnant women were excluded from the study. Patients or their parents were fully questioned regarding age, site, duration, occupation, residence, associated symptoms (such as itching and pain), associated diseases (like atopic dermatitis), topical steroid usage and history of molluscum contagiosum in other family members.

Physical examination was carried out regarding site, size and number of lesions. Pre-and post-treatment photographs were taken using Cyber-Shot Sony-digital, high sensitivity, 7.2 mega pixels, in the same place with fixed illumination and distance.

The procedure was fully described to the patients or their parents and consent were obtained from all participants in this study. This study was approved ethically by the Scientific Committee of Dermatology and Venereology of the Arab Board for Medical Specializations.

**Treatment protocol**

The 20% KOH was prepared by dissolving 20 gm of KOH crystal in 100 cc of distal water.
The patients had been equally divided into 3 groups; each of them consists of 30 patients.

Group 1: patients were treated by topically applied 20% KOH by wooden stick daily at night (first application done by physician and then by patient after providing full information; till the lesion inflame, ulcerate, crusted or disappear but for not more than one month).

Group 2: patients were treated by pricking the lesion with 27 G needle dipped in 20% KOH weekly. (Done by physician till the lesion inflame, ulcerate, crusted or disappear but for not more than four sessions).

Group 3: patients were treated by pricking the lesion with 27G needle weekly (done by physician till the lesion inflame, ulcerate, crusted or disappear but for not more than four sessions).

The treatment sessions were done at the time of presentation and then every week until either complete cure was achieved, or maximum of four sessions was achieved.

Follow up
The patients were seen regularly every week for 1 month during the treatment period. At each visit the response to treatment was assessed according to the change in size, number development of new lesions. The side effects of treatment modalities were recorded such as burning, erythema, scar formation and signs of secondary bacterial infection (pain, tenderness, erythema and swelling). Then the patients were followed up for two months from the last treatment session for any sign of relapse.

Assessment of response
1. Complete cure: disappearance of all lesions in the treatment period.
2. Moderate improvement: disappearance of more than 50% of lesions.
3. Slight improvement: disappearance of less than 50% of lesions.
4. No response: persistence of all lesions throughout treatment period.
5. Relapse: appearance of new lesion(s) in the previously healed site.

Statistical analysis
Statistical analysis was done by using the chi-square. P-value of less than 0.05 was considered to be significant.

Results
A total of ninety patients were enrolled in this study. Thirty one of them defaulted after the first visit for unknown reasons; two patients were excluded from the study (group 1) because of side effects; and the remainder 57 patients completed the study. Total number of treated lesions was 488. Of those patients completed the study, 31 (54.3%) were males and 26 (45.6%) were females with male to female ratio of 1.19:1. Their ages ranged from 1.5-62 years (mean 19.4±16.7 SD). The most common age group affected was 2-12 years which included 29 (50.8%) patients, Figure 1.

The duration of disease ranged from 1-7 months. Nine (15.7%) patients had more than one anatomical sites involved. The most common involved sites were the face and neck 49 (85%) patients, trunk 8 (14%) patients, extremities 3 (5.2%) patients and genital and perianal areas 6 (10.5%) patients, Figure 2. Thirteen (22.8%) patients had been associated with different types of atopy; (atopic dermatitis, asthma and hay fever).

Group 1 (topical 20% KOH applied daily)
Thirty patients, 10 of them defaulted for unknown reason and other 2 patients developed side effects. The remaining 18 patients were treated by topically applied 20% KOH. Their ages ranged from 1.5-51 years, (mean 18.8±16.2 SD). There were 10 males and 8 females with male to female ratio of 1.25:1. Total number of treated lesions was 124. During the treatment period 2 (11%) patients were completely cured after the first week of treatment, 5 (27%) patients required another week and 10 (54%) patients healed after the fourth week. one (6%) patient did not respond completely. The p-value was highly significant (=0.0019) (Table 1).
The reported side effects in this group were (Table 2):

1. Mild pain in 11 (55%) patients.
2. Mild burning sensation in 4 (20%) patients.
3. Secondary bacterial infection in 2 (10%) patients.

**Group 2 (topical 20% KOH with pricking weekly)**

Thirty patients, 7 defaulted for unknown reasons and 23 patients were treated by 20% KOH with pricking. Their ages ranged from 2-47 years (mean 19.4±16.1 SD). They were 13 males and 10 females with male to female ratio of 1.3-1. Total number of treated lesions was 193. The duration of disease ranged from 1-7 months. After one session of treatment 1(4%) patient was completely cured, 11 (47%) patients needed another week of treatment and 8 (35%) patients were cured at the end of the fourth week. At the end of the treatment period 3 (13%) patients were still having lesions. The p-value was highly significant (<0.001), Table 1.

The reported side effects were (Table 2):
1. Mild pain in 8 (34.7%) patients.
2. Burning sensation in 2 (8.6%) patients.

**Group 3 (Pricking weekly)**

Thirty patients, 14 defaulted for unknown reasons and 16 patients were treated by pricking only. Their age ranged from 4-62 years (mean 22.2±18.5 SD). They were 8 males and 8 females with male to female ratio 1-1. Total number of treated lesions was 171. The duration of disease ranged from 1-4 months. After one session none of the patients was cured completely, 3 (18%) patients required two sessions and 9 (56%) patients needed another session to accomplish complete healing, while 4 (25%) patients still have lesions. The p-value was highly significant (<0.0014), Table 1. The reported side effects are shown in Table 2. Mild pain was noticed in 3 (18.7%) patients.

During the follow up period, scarring and relapse were not reported in any of the patients in the three groups. When the results of treatment of the three groups were compared with each other, there was no statistical difference. (p-value < 0.05).

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**Table 1:** Rate of complete cure during the period of treatment.

<table>
<thead>
<tr>
<th>Treatment Groups</th>
<th>1st week No %</th>
<th>2nd week No %</th>
<th>4th week No %</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=18)</td>
<td>2 (11)</td>
<td>7 (38)</td>
<td>17 (94)</td>
<td>P = 0.0019</td>
</tr>
<tr>
<td>Group 2 (n=23)</td>
<td>1 (4)</td>
<td>11 (47)</td>
<td>20 (86)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Group 3 (n=16)</td>
<td>0 (0)</td>
<td>3 (18)</td>
<td>12 (75)</td>
<td>P = 0.0014</td>
</tr>
</tbody>
</table>

**Table 2:** Side effects of the treatment modalities.

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>11 (55%)</td>
<td>8 (34%)</td>
<td>3 (18, 7%)</td>
</tr>
<tr>
<td>Burning</td>
<td>4 (20%)</td>
<td>2 (8.6%)</td>
<td>None</td>
</tr>
<tr>
<td>Secondary bacterial infection</td>
<td>2 (10%)</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

**Discussion**

The findings of this study regarding male to female ratio (1.19-1), most common age group affected (2-12 years) and number of lesions (1-26) were similar to published data in an Indian study [44], an American study [37] and an Italian study [45] respectively.

Most MC lesions were extra genital, apart from 6 (10.5%) patients who had genital and perianal lesions. Of those 6 patients, 3 (5.2%) patients had lesions confined only to the genital area, 2 of them were adults and the other was child with the possibility of sexual abuse; and the other 3 (5.2%) patients had lesions in other body parts such as the face and trunk in association with the involvement of the genital area as a part of generalized involvement rather than sexually transmitted disease.

Forty nine (85.9%) patients had their lesions on the face and neck; of which 41 (71%) patients on left side, which is the most common site involved in the body. Twenty two (38.5%) were children and 27 (47.3%) were adults. These adult patients had their lesions on the beard area; pointing to the possibility that they acquired the infection after kissing, shaving and shaving. In a British study the trunk was the most common site involved (74%) and the involvement of the genital area was more common than what was found in the present work; this might be due to differences in social habits and promiscuous relations [33]. Associated diseases noted were mainly atopy in 13 (22.8%) patients. Of these, 7 (12.2%) patient had atopic dermatitis and the remainder patients had asthma and hay fever; while in other studies atopic dermatitis was seen in 17-25% of patients with MC [33,84].

The present work showed that the duration of disease ranged from 1-7 months and this finding is approximate to other studies in which the duration ranged from 1-12 months [33,37,46].

The disease is self-limited but this might takes several months to years [1]. Accordingly, the disease should be treated to clear the lesions as quick as possible due to cosmetic impact on the patient and also to limit the spread of the disease.

There is no specific treatment for MC, although various surgical and medical strategies were used with different success rates and various side effects with longer duration of therapy such as curettage, cantharidine and 5% imiquimod cream. Curettage cure rate was 80%, used once and repeated as needed; pain and scarring were common side effects [33]. Imiquimod cure rate was 75-82%, used 3-5 times/ week for 5-9 weeks; it is expensive and associated with erythema, pruritus, post inflammatory pigmentation and ulceration [42].

While the present study using topical 20% KOH daily, 20% KOH with pricking and pricking only once weekly showed cure rates of 94%, 86% and 75% respectively after 4weeks of treatment, the reported side effects were mild pain due to pricking, mild burning sensation and transient erythema and secondary bacterial infection which required only topical antibiotic. Scarring and relapse were not reported in all of the patients.

So the present work has shown high cure rates with shorter duration of treatment and mild side effects. Surprisingly, pricking of lesions by 27 G needle alone was as effective as other therapies,

(p<0.05), and this is very interesting point as pricking only might induce inflammation and stimulate the immune system through releasing relevant cytokines and other immune enhancers and thereby attraction of immune cells (T-cells) which are important in clearing of the MC lesions.

Conclusions and Recommendations

1. Pricking MC lesions by 27 G needle alone is safe, highly effective and stimulating mode of therapy. The present work opened a new era of therapy that doesn’t necessitate using any chemical agent or drug.

2. Still topical 20% KOH alone or with pricking are new and effective modes of treatment.

3. Further studies are recommended to clarify the mechanism of action of pricking by combining histopathological assessment during the resolution phase.

Acknowledgment

The authors would like to acknowledge the tremendous contribution of personnel and colleagues in the Dermatology Clinic and the Central Laboratory in Kufa Medical School Teaching Hospital for their assistance in completing this work. Also great thanks are presented to all patients and healthy controls recruited in this study for their kind cooperation.

References


