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Study of Topical Potassium Hydroxide versus Candida Antigen Immunotherapy for Molluscum Contagiosum Management

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ABSTRACT

Background: Molluscum Contagiosum (MC) has no FDA-approved treatments as of yet. Although many other treatments have been suggested, the majority of the efficacy evidence comes from modest case studies.

Objectives: The aim of the current work was to evaluate the safety as well as efficacy of intralesional candida Ag immunotherapy versus topical KOH (10 %) in the treatment of MC.

Patients and methods: A total of 40 patients (21females and 19 males) with multiple lesions of MC. They were divided into two equal groups at random; **group 1** treated by candida antigen at 2 weeks intervals with a maximum of five injections or clinical cure. **Group 2** subjected to topical 10% KOH twice daily for ten weeks.

Results: Complete clinical response was attained in 80% of MC patients who treated with candida antigen for 10 weeks versus 85% of patients who treated with topical KOH for 10 weeks, while 20 % of patients showed no response in group 1 versus 5% in group 2 after the end of therapy. without recurrence after 3 months in all patients demonstrating complete reaction. In group 1, most patients tolerated the side effects, which in 5% of cases manifested as erythema and hyperpigmentation. While in group 2, hypopigmentation (15%), hyperpigmentation (10%), pruritus (10%) during treatment were reported. There was significant reported burning sensation among 25% of patients treated with topical potassium hydroxide (P = 0.047).

Conclusion: It could be concluded that both topically applied KOH10% and intralesional candida are dependable, less expensive treatments for non-genital MC.

Keywords: Potassium Hydroxide, Candida Antigen Immunotherapy, Molluscum Contagiosum.

INTRODUCTION

The molluscum contagiosum (MC) virus is the source of the self-limiting cutaneous viral illness known as molluscum contagiosum (MC). Children and patients with compromised immune systems are more susceptible to this virus. According to reports, 5.1-11.5 percent of pediatric patients have MC, with warm climates accounting for the majority of cases **(1).**

Beginning in the early nineteenth century, Bateman first described MC and then gave it a name. The intracytoplasmic inclusion bodies—also known as Molluscum or Henderson-Paterson bodies—were first characterized by Henderson and Paterson in 1841 **(2)**. Julinsberg **(3)**, was able to extract filterable virus from lesions and demonstrate transmissibility at the beginning of the twentieth century. Later, Hanson and Diven discussed the similarities between vaccinia and molluscum **(4).**

Clinical images are characterized by 2–5 mm-diameter papules with a central umbilication that are dome-shaped, smooth-surfaced, pearly, skin-colored, or white. However, atypical MC presentations can make it difficult for clinicians to make a diagnosis. Immunosuppressed patients are more likely to experience immunotypical presentations, such as large, cystic, ulcerated, or condyloma acuminatum-like lesions **(5).**

There are no FDA-approved treatments for MC as of now. Although many other treatments have been suggested, the majority of the efficacy data come from uncontrolled research and small case series **(5).**

Treatment options for MC include physical eradication via curettage or cryotherapy, systemic therapy with cimetidine, and topical therapies using cantharidin, salicylic acid, podophyllotoxin, tretinoin, imiquimod, or potassium hydroxide (KOH)**(6).**

A dead yeast protein is injected intralesionally into the MC lesions as part of candida antigen immunotherapy. It is hoped that once the immune system becomes active in this area, it will produce an immunological response against the wart or MCV in addition to the yeast protein. Instead of treating each lesion locally, this triggered immune response might then result in the destruction of all lesions on the body**(1).**

Evaluation of the efficacy and safety of intralesional candida Ag versus topical KOH (10 %) in the treatment of MC. was the goal of this study.

PATIENTS AND METHODS

The current study included 40 patients (21females and 19 males) with multiple lesions of MC referred to the Outpatient Clinic, the Dermatology and Venereology Department, Zagazig University Hospitals.

Inclusion criteria: Male and female patients, determined clinically to have MC, aged 2-18 years.

Exclusion criteria: Prior unfavorably susceptible reaction to candida antigen, pregnant and lactating female, acute febrile disease, asthma or a skin condition that makes them more sensitive, iatrogenic or essential immunosuppressed understanding, patient getting any treatment of MC amid the most recent month, any summed up dermatitis, and genital MC.

Every patient was subjected to:

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1. Complete cautious history taking including: individual history, present history, family history, span of MC, past treatment, history of bronchial asthma, nourishment or medication sensitivity, systemic sickness, or immunosuppressive medication consumption.
2. Full clinical and dermatological examination including:
   a. General physical examination.
   b. Local examination of skin injuries including number, size, site, sort, and other related skin sores. Patients were told not to utilize whatever other MC treatment amid the study time frame.

The patients were divided into 2 groups as indicated by methodology of treatment utilized:

Group 1: included 20 patients subjected to intralesional immunotherapy utilizing candida albicans antigen. (Candida albicans 1:20 w/v 10 ml vial, Allergy Laboratories, Inc. Oklahoma City, USA)

Before injection therapy, 0.1 milliliters of Candida antigen were injected intradermally into the skin of the forearms of all patients to check for preexisting immunity to antigen preparation. Erythema and induration of at least 5mm diameter within 48–72 hours are necessary for the determination of a positive reaction [7].

Responders to intradermal skin testing were subjected to immunotherapy by an injection of 0.3 ml of 1/1000 solution of Candida antigen (Candida albicans 1/1000, 2.5 ml vial brought from Allergy and Immunity Unit, Ain Shams University Hospitals) utilizing an insulin syringe 1 ml and a 30G needle directly into the largest molluscum lesion. For patients with exclusively small lesions, up to three largest lesions will be injected to deliver the full volume and fill the treated molluscum papule(s).

Group 2: included 20 patients with non-genital molluscum and were examined clinically and photographed before and after they had been treated with topical application of 10% KOH solution daily at night for total duration of 8 weeks.

Preparation and method of application of the solution:

Ten grams of KOH were dissolved in 100 ml of purified water, and each patient received a bottle of the solution. Patients or their parents were instructed to use a cotton swab to gently apply the agent topically twice daily, at home, to MC lesions while avoiding leakage onto healthy skin for 2 to 10 weeks, or until the lesions are cleared. In an outpatient setting, the therapeutic drug was first applied to teach patients how to utilize it properly at home. All patients were required to visit the outpatient clinic every two weeks for evaluation. Regular attendance was emphasized as being crucial to avoid defaulting.

Photographs of lesions in all patients at follow-up visits were taken to evaluate the clinical response.

Analyzing the clinical outcome:

Lesson count reduction and photographic comparisons between each visit and the baseline images were used to assess treatment response in the two groups. After each treatment session, adverse effects were also assessed.

Following was an evaluation of the reaction [7]:

• Complete response: if the lesions completely vanished and the skin marks return to normal.

• Partial response: If there was a clearance of more than 50% of lesions relative to the total number of lesions

• If the lesions had been cleared by less than 50%, there will be no reaction.

Follow-up: Following the termination of treatment, follow-up was conducted through clinic visits every visit and every month for three months to look for any recurrence.

Ethical consent:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University (IRB Approval Number (4313/4-2-2018)). Written informed consent was taken from all participants. The study was conducted according to the Declaration of Helsinki.

Statistical analysis

In order to analyze the data acquired, Statistical Package of Social Services version 20 was used to execute it on a computer (SPSS). In order to convey the findings, tables and graphs were employed. The quantitative data was presented in the form of the mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t test (T) is used to assess the data while dealing with quantitative independent variables. Pearson Chi-Square and Chi-Square for Linear Trend (X^2) were used to assess qualitatively independent data. The significance of a P value of 0.05 or less was determined.

RESULTS

Table 1 shows the demographic characters. The studied patients of group 1 were 14 females (70.0%) and 6 males (30.0%), patients mean age was 4±1.8years and ranged from (2.5-17) years. The studied patients The studied patients of group 2 were 7 females (35.0%) and 13 males (36.0%), patients mean age was 4±1.8 years and ranged from (2-9) years, the difference statistically significant of both groups regard age, sex $p<0.05$ **(table1).**

Table (1): Demographics

	Candida antigen immunotherapy group (n.20)	Topical potassium hydroxide group (n.20)	Test of sig	p-value
Age (years) • Mean ± SD • Median • (range)	7.6±5.3 5 (2.5-17)	4±1.8 3.5 (2-9)	U 2.203	.028(S)
Sex • Females • Males	14(70.0%) 6(30.0%)	7(35.0%) 13(65.0%)	χ^2 4.9	0.027(S)

Patients of group 1 were treated by Candida antigen immunotherapy, the mean duration of disease was 3.3±2.1 and ranged from (1-8) month. The mean number of lesion was 4.4±3.7 and ranged from (1-13). Site of molluscum contagiosum lesions distributed as follow; (50%), of patients had lesion in face,15% patients had lesion in back, similar percent had lesion in upper limb. Where (10%), (5%), (5%), had lesion in neck, chest, abdomen respectively.

Patients of group 2 were treated by topical potassium hydroxide; the mean duration of disease was 2.4±1.4 and ranged from (1-6) month. The mean number of lesion was 5.8±4.02 and ranged from (1-13). Site of molluscum contagiosum lesions distributed as follow; (60%), of patients had lesion in face,20% patients had lesion in abdomen, Where;(5%) of patients, had lesion in each of following site neck, chest, upper limb, lower limb, buttock.
Regarding the aforementioned clinical characteristics, group 1 and group 2 do not significantly differ from one another**.** p>0.05 **(table 2).**

Table (2): Clinical characters of the studied patients

	Candida antigen immunotherapy group (n.20)		Topical potassium hydroxide group (n.20)		χ^2	p-value
	No.	%	No.	%		
• Disease duration (month) Mean ± SD Median(range)	3.3±0.73 2(1-8)		2.4±0.4 2(1-6)		U 1.14	0.254
• Number of lesion Mean ± SD Median(range)	4.4±1.01 3(1-13)		5.8±1.02 5(1-13)		U 1.16	0.246
Site of lesion						
• Chest	1	5.0	1	5.0	f	1
• Abdomen	1	5.0	4	20.0		0.34
• Back	3	15.0	0	0.0	f	0.23
• Upper limb.	3	15.0	1	5.0	f	0.61
• Lower limb	0	0.0	1	5.0	f	0.99
• Face	10	50.0	12	60.0	0.404	0.53
• Neck	2	10.0	1	5.0	f	0.99
• Buttock	0	0.0	1	5.0	f	0.99

There was statistically significant longer duration of treatment and number of treatment sessions for topical potassium hydroxide group p=0.0001 (Table 3).

Table (3): Comparison of studied treatment modalities regarding, duration of treatment and number of treatment sessions

	Candida antigen immunotherapy group (n.20)	Topical potassium hydroxide group (n.20)	u	p-value
• Duration of treatment(week) Mean ± SD Median(range)	7.2±1.7 7(2-10)	10±0 10(10-10)	4.02	0.0001(S)
• Number of treatment sessions Mean ± SD Median(range)	3.6±1.4 4(1-5)	10±0 10(10-10)	5.82	0.0001(S)

u =Mann-Whitney U test

Adverse effect of Candida antigen immunotherapy treatment, represented as hyperpigmentation, and erythema among 5% of patients. While 15%, 10%,10% topical potassium hydroxide group reported hypopigmentation, hyperpigmentation, pruritus during treatment. There is significant reported burning sensation among 25% of patients treated with topical potassium hydroxide (P = 0.047) (Table 4).

Table (4): Adverse effect of studied treatment modalities

	Candida antigen immunotherapy group (n.20)		Topical potassium hydroxide group (n.20)		f	p-value
	No.	%	No.	%		
Adverse effect						
• Hyperpigmentation	1	5.0	2	10.0	f	0.99
• Hypopigmentation	0	0.0	3	15.0	f	0.23
• Pruritus	0	0.0	2	10.0	f	0.49
• Burning sensation	0	0.0	5	25.0	f	0.047(S)
• Flu like symptoms	0	0.0	0	0.0	-	-
• Pain	0	0.0	0	0.0	-	-
• Blistering	0	0.0	0	0.0	-	-
• Erythema and edema	1	5.0	0	0.0	-	0.99

f=Fisher exact test

Table 5 shows that neither of the two treatment modes significantly differed in terms of the therapeutic response. p>0.05 (table 5).

Table (5): Therapeutic response of the studied patients regarding treatment modalities

	Candida antigen immunotherapy group (n.20)		Topical potassium hydroxide group (n.20)		χ^2	p-value
	No.	%	No.	%		
Therapeutic response						
• Complete	16	80.0	17	85.0		
• Partial	0	0.0	2	10.0	3.8	0.15
• No response	4	20.0	1	5.0		

Table 6 shows that there was no significant correlation between sex, disease length per month, number of lesions, number of treatment sessions, duration of treatment per week, and site of lesions and the therapeutic response with Candida antigen immunotherapy. Older individuals, however, demonstrated a substantial competitive reaction, p=0.003 (Table 6).

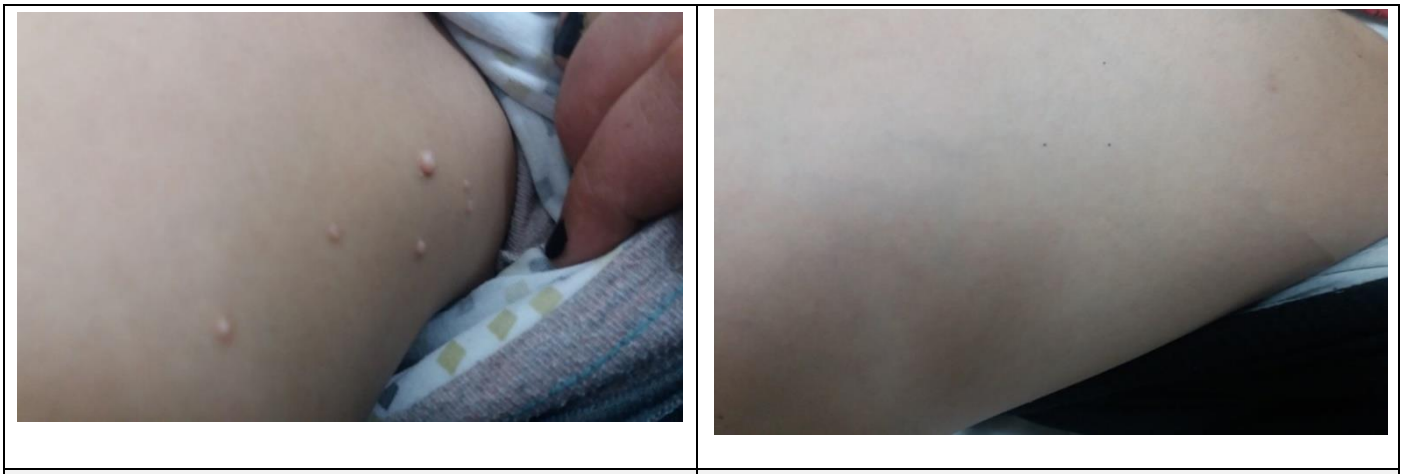
Table (6): Relation between therapeutic response of treatment with Canndida antigen immunotherapy group and their basic characters (n.20)

Variables			Candida antigen immunotherapy group (n.20)		u/ χ^2	p
			complete n.16	No response n.4		
Age (years)		Median(range)	6(3-17)	2.8(2.5-3)	2.95	.003(S)
Sex	Females	N	11	3	0.06	0.81
		%	68.8%	75.0%		
	Males	N	5	1		
		%	31.3%	25.0%		
Disease duration per month		Median(range)	2(1-8)	2.5(2-5)	0.147	.883
Number of lesion		Median(range)	3.5(1-13)	3(2-13)	0.336	.737
Site of lesion	Chest	N	1	0	f	0.99
		%	6.3%	0.0%		
	Abdomen	N	1	0	f	0.99
		%	6.3%	0.0%		
	Back	N	3	0	f	0.99
		%	18.8%	0.0%		
	Upper limb	N	1	2	f	0.088
		%	6.3%	50.0%		
	Lower limb	N	0	0		
		%	0.0%	0.0%		
	Face	N	8	2	0	1
		%	50.0%	50.0%		
	Neck	n	2	0	f	0.99
		%	12.5%	0.0%		
	Buttock	N		0		
		%	0.0%	0.0%		
Number of treatment session		Median(range)	4(1-5)	4(3-5)	0.099	.921
Duration of treatment per week		Median(range)	7 (2-10)	7(6-10)	0.099	.921

Table 7 shows that Age, sex, disease duration per month, number of lesions, number of treatment sessions, length of therapy per week, and location of lesions did not significantly affect the therapeutic response to topical potassium hydroxide. $p>0.05$ (Table 7).

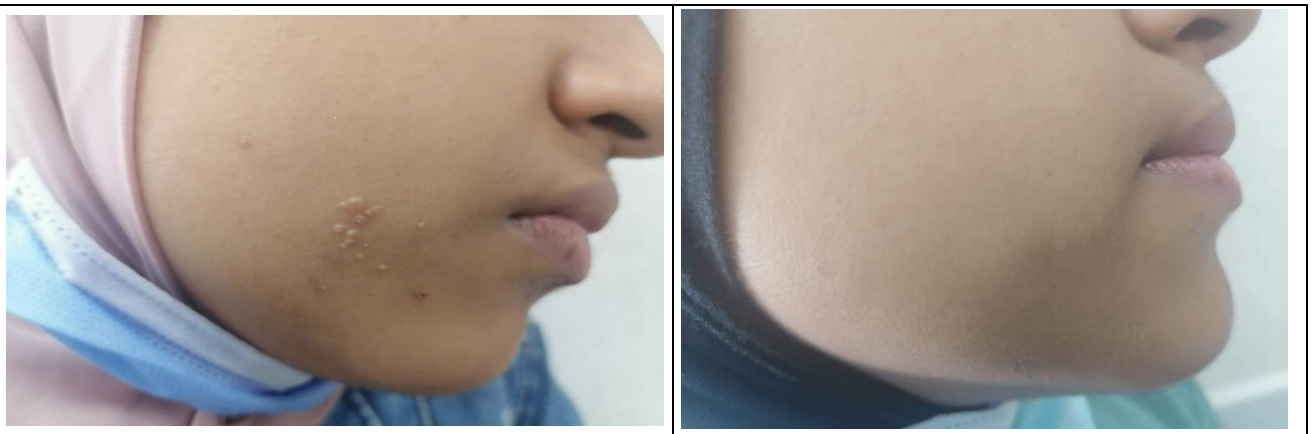
Table (7): Relation between therapeutic response of treatment with Topical potassium hydroxide group and their basic characters (n.20)

Variables			Topical potassium hydroxide group (n.20)			KW/ χ^2	p
			complete n.17	Partial response n.2	No response n.1		
Age (years)		Median(range)	4.(2-9)	4.5(3-6)	2(2-2)	2.32	.314
Sex	Females	N	7	0	0	1.9	0.39
		%	41.2%	0.0%	0.0%		
	Males	N	10	1	2		
		%	58.8%	100.0%	100.0%		
Disease duration per month		Median(range)	2.(1-6)	1.5(1-2)	4(4-4)	2.89	.236
Number of lesion		Median(range)	4(1-13)	7(7-7)	10(10-10)	1.62	.446
site of lesion	chest	N	1	0	0	0.18	0.91
		%	5.9%	0.0%	0.0%		
	Abdomen	N	4	0	0	0.88	0.64
		%	23.5%	0.0%	0.0%		
	Back	N	0	0	0		
		%	0.0%	0.0%	0.0%		
	Upper limb	N	1	0	0	0.18	0.91
		%	5.9%	0.0%	0.0%		
	Lower limb	N	1	0	0	0.18	0.91
		%	5.9%	0.0%	0.0%		
	Face	N	9	1	2	2.3	0.81
		%	52.9%	100.0%	100.0%		
	neck	N	1	0	0	0.18	0.91
		%	5.9%	0.0%	0.0%		
	Buttock	N	1	0	0		
		%	5.9%	0.0%	0.0%		
Number of treatment session		Median (range)	10(10-10)	10(10-10)	10(10-10)	.000	1.0
Duration of treatment per week		Median (range)	10(10-10)	10(10-10)	10(10-10)	.000	1.0



(A) Before | (B) After

Fig. (1): A case of MC (5 years old male) showing complete response To KOH % after ten weeks



(A) Before | (B) After

Fig. (2): A case of MC (13 years old female) showing complete response To Candida after five sessions

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DISCUSSION

Children are most affected by Molluscum contagiosum (MC), a common cutaneous infection brought on by a DNA poxvirus. The MC virus has been modified to thrive in epidermal keratinocytes, where it replicates and produces localized lesions made up of hyperplastic epithelial cells. It takes between two and eight weeks after the initial vaccination for lesions to manifest themselves on the epithelial surface [(8)].

Treatment choices incorporate damaging treatments (cantharidin, curettage, keratolytics, cryotherapy, among others), insusceptible modulators (cimetidine, imiquimod), and antivirals (cidofovir). The majority of these strategies are tedious, have numerous unfriendly impacts like bothering, aggravation, scarring and post provocative hyperpigmentation with unsuitable results [(9)].

This study's goal was to examine the effectiveness and safety of topical 10 percent KOH and intralesional candida antigen for treating MC.

In this study twenty patients (group1) were treated with candida antigen and twenty patients (group 2) were treated with topical 10% KOH.

In group (1) sixteen patients (80%) showed a complete response to therapy with candida antigen and four patients (20%) showed no response after 4-5 sessions of intralesional candida antigen without recurrence after 3 months in all patients demonstrating complete reaction.

The response rate with candida antigen in our study was nearly similar to that reported by **Nofal *et al.*** [(10)] who have treated 68 patients with common and planter warts with MMR versus candida antigen. He reported (73.5%) clearance after use candida antigen compared with the MMR group (67.7%).

The response rate in our study was higher than that reported by **Enns and Evans** [(11)] who have treated 29 patients with multiple MC lesions with intralesional candida antigen and showed complete response in 16 (55.2%) of them, partial response in 11(37.9%) of them and two (6.9%) had no improvement. The overall response rate was 93%.

Similarly, **Thomas *et al.*** [(12)] in treatment of recalcitrant molluscum contagiosum in a stem cell transplant patient with candida immunotherapy, showed (100%) complete clearance.

In contrast to our results **Gamil *et al.* [7]** reported complete clearance in 50% of MC patients after intralesional immunotherapy with Candida antigen.

In group (2) Two patients (10%) had a partial response to treatment with KOH10%, one patient (5% showed no response), and seventeen patients (85%) showed a complete response. Since 1999, several doses of KOH solution (2.5–20%) have been tested to treat MC. Similarly, **Qureshi *et al.* [13]** reported complete clearance of MC lesions after topical 10% KOH twice daily in **80%.**

Similarly, **Chathra *et al.* [14]** and **Rahman [15]** reported complete clearance of MC lesions after topical 10% KOH once daily in 85% and 71.4% of patients after 12 weeks respectively, pigmentary disturbance were a common side effect.

On the contrary of our study, Muzaffar and Faiz [16] reported complete remission in 41.2% of 17 MC patients treated with topical 10% KOH solution once daily for two weeks versus 25% partial remission only with 5% KOH topical solution.

The majority of participants in our study were able to handle the side effects, adverse effects of candida antigen immunotherapy treatment, represented hyperpigmentation and erythema among 5% of patients. While in topical potassium hydroxide group reported hypopigmentation (15%), hyperpigmentation (10%), pruritus (10%) during treatment.

There is significant reported burning sensation among 25% of patients treated with topical potassium hydroxide (P = 0.047).

These side effects were similar to these detected by **Mahajan *et al.* [17]** that reported complete clearance in 100% of MC patients treated with topical 20% KOH solution

CONCLUSION

It could be concluded that both topically applied KOH10% and intralesional candida are dependable, less expensive treatments for non-genital MC.

Because of its keratolytic effect and daily usage at home, topical KOH is 10% effective, painless, and non-invasive. Candida antigen intralesional immunotherapy is a successful treatment, particularly for generalized non-genital MC lesions in reluctant individuals. The advantage of the accepted manuscript is that there is no scarring and injection only in one or two lesions, not all lesions.

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