A comparative study of 10% KOH solution and 5% imiquimod cream for the treatment of *Molluscum contagiosum* in the pediatric age group

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ABSTRACT

Background: Although *Molluscum contagiosum* (MC) is a self-limiting condition, active therapy could prevent further spread and improve cosmesis. Most of the available treatment modalities traumatize the lesions and have to be undertaken in the hospital, therefore evoking panic in children. In the quest for an alternative therapy, this study comparing 10% potassium hydroxide (KOH) solution and 5% imiquimod cream was taken up. **Aims and Objectives:** To compare the efficacy and tolerability of 10% KOH and 5% imiquimod in the treatment of MC. **Materials and Methods:** This comparative study was conducted over a period of 18 months from October 2011 to March 2013, 40 patients between the age group of 1-18 years with clinically diagnosed MC were divided into two groups (lottery method), 20 patients were treated with 5% imiquimod cream (Group A) and the other 20 were treated with 10% KOH solution (Group B). Patients were followed up on the 4th, 8th and 12th week of treatment. **Results:** At the end of 12 weeks, out of 20 patients who received 10% KOH, 17 patients showed complete disappearance, whereas out of 20 patients who received 5% imiquimod, only 10 patients showed total clearance of the lesions. Adverse events were more frequent with 10% KOH, pigmentary disturbances being the most common. **Conclusion:** With only minor adverse effects, 10% KOH is an inexpensive and efficient modality for the treatment of MC in the pediatric age group. Although 5% imiquimod was effective in clearing the lesions with minimal adverse effects, the longer duration required for its efficacy may deter its wider use.

Key words: 5% imiquimod, 10% potassium hydroxide, *Molluscum contagiosum*

INTRODUCTION

Molluscum contagiosum (MC) is a commonly encountered cutaneous viral infection in children, its hallmark being spontaneous resolution.[1] Despite its benign nature, active therapy may be desirable to prevent further spread, relieve symptoms, prevent scarring, and for cosmetic, and social reasons.[2] Parental concern is valid as these lesions appear unsightly and the affected children may face isolation by their peers.[3] Treatment modalities include: Mechanical destruction by curettage, cryotherapy or evisceration; chemical destruction of the lesions using potassium hydroxide (KOH) or cantharidin; immunomodulatory agents such as topical imiquimod, tretinoin and oral cimetidine; and the antiviral agent cidofovir.[4] In spite of options galore, no single therapy has consensus approval for the treatment of MC in the pediatric age group. Mechanical destruction of lesions is the easiest method among adults, but in children, owing to fear and lower tolerance of pain, these methods cannot be used routinely.[5] Studies examining response to laboratory pain stimuli in children have shown that Asians demonstrated more pain sensitivity compared to other ethnic groups.[6] Furthermore, parents do not favor frequent visits to the hospital as children exhibit high levels of anticipatory anxiety. Thus, there is a need for a therapeutic modality that can be used at home and is not painful.[7]

Potassium hydroxide acts by dissolving the keratin and destroying the skin. It has been used in various concentrations, that is, 5%, 10%, and 20%, for the treatment of MC.[8] 10% KOH has the dual advantage of safety and efficacy.[9]

Imiquimod is a tissue response modifier that induces interferon-α, a potent antiviral agent. It has been shown to possess an excellent safety profile in the treatment of cutaneous viral diseases.[10,11]

Taking this into consideration, we undertook a randomized comparative study to assess and compare the efficacies of 10% KOH aqueous solution and 5% imiquimod cream for the treatment of MC in the pediatric age group.

MATERIALS AND METHODS

After obtaining permission from the Institutional Ethics Committee, 40 patients between the age group of 1-18 years with minimum 3 lesions of MC were recruited to this study. Patients with eyelid involvement, secondary infection and history of hypersensitivity to imiquimod were not enrolled in the study. Written informed consent was obtained. Details of symptoms, duration, family history, site, and number of lesions were recorded.

Patients were divided by the lottery method into two groups; A and B, each containing 20 patients. Patients in Group A were given 5% imiquimod cream in 0.25 g sachets (Galderma) and their parents advised to apply it as a thin layer, rubbing it until it was no longer visible. Patients in Group B were given 10% KOH solution with instructions to the parents to apply using a tooth pick after covering the surrounding area with petrolatum and avoid any spillage over normal skin. Both groups were advised to apply the respective agents at night and wash off in the morning, 3 times a week for 12 weeks or until the lesions cleared, whichever was early.

Photographs were taken before and after treatment. The importance of regular attendance was stressed upon all the patients to prevent defaulting.

Patients were followed up at 4th, 8th and 12th week of treatment. On each visit, clinical response to treatment, efficacy, and tolerability parameters were evaluated. The clinical response to treatment was graded as complete clearance, partial clearance and no change. Data were analyzed using Chi-square test, Fishers exact test and Friedman test, whereas pairwise comparison was done by Wilcoxon signed rank test and Mann-Whitney test. The results were presented in the form of frequency table and graphs.

RESULTS

All the 40 patients adhered to the treatment given to them in our study. Maximum number of cases were in the age group of 5-10 years (42.5%) and females 24/40 (60%) outnumbered males 16/40 (40%). There was no significant variation between the two groups in terms of age and gender. A positive family history was obtained in 18 of the 40 patients (45%). Only three patients gave history of atopy, out of which 2 patients had eczema surrounding the lesions. Most common site of occurrence was the face followed by chest and neck, which were involved in 22, 9, and 6 patients, respectively.

At the end of this study, Group A showed complete clearance of lesions in 10 (50%) out of the 20 patients, with none showing clearance by 4 weeks, 2 patients showing complete clearance by 8 weeks and the rest by 12 weeks. Group B showed total clearance of lesions in 17 (85%) out of 20 patients, out of which 2 patients were cleared of lesions by 4 weeks, another 5 by the end of 8 weeks and 10 more patients by 12 weeks [Figure 1].

Initial distribution of number of lesions was statistically similar between two groups with P = 0.470. A steady decline in the mean value of the lesions was noted in both the study groups throughout the follow-up period. The mean lesional count decreased from 7.20 ± 3.381 standard deviation (SD) to 0.90 ± 1.294 SD at the end of 12 weeks in patients treated with imquimod [Figure 2-4]. The comparison between the number of lesions at baseline and the number of lesions at week 12 was found to be statistically significant with P = 0.000 in Group A patients. The mean lesional count decreased from 7.10 ± 5.057 SD to 0.20 ± 0.523 SD at the end of 12 weeks with 10% KOH solution [Figure 5-7]. This reduction in the number of lesions at the end of 12 weeks was statistically significant P = 0.000 in Group B patients.

Overall, a better response was shown by patients who received KOH as compared to those who received imiquimod, and the difference was statistically significant as P = 0.010 at 1st and 2nd follow-up; and P = 0.019 at the last follow-up [Table 1].

Five (25%) of 20 patients receiving imiquimod developed new lesions whereas no new lesions were seen in those who received KOH. The difference was statistically significant (P = 0.024).

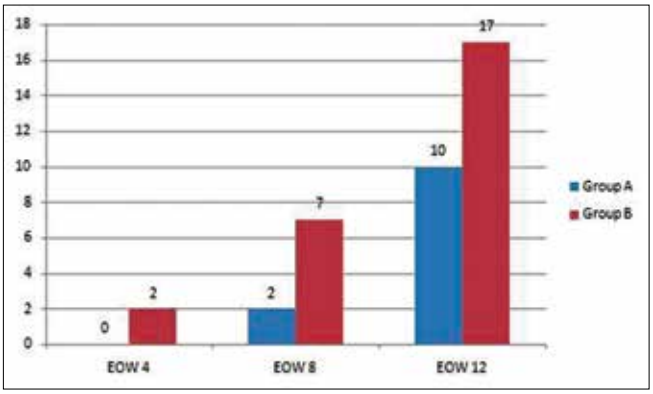

Figure 1: Number of patients who showed complete disappearance of lesions

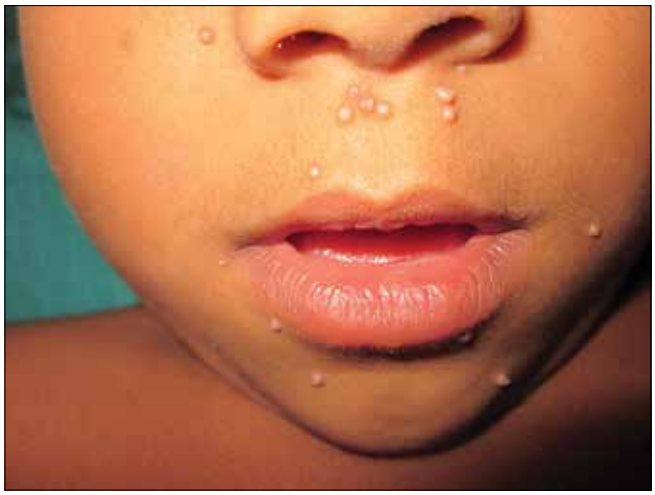

Figure 2: Pretreatment

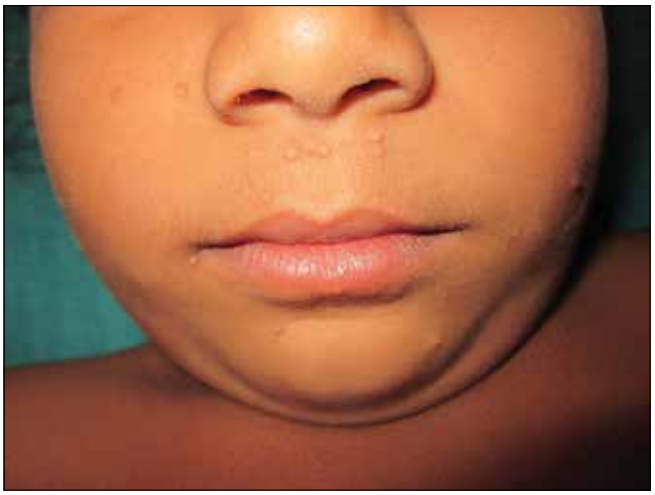

Figure 3: Disappearance of lesions following treatment with imiquimod

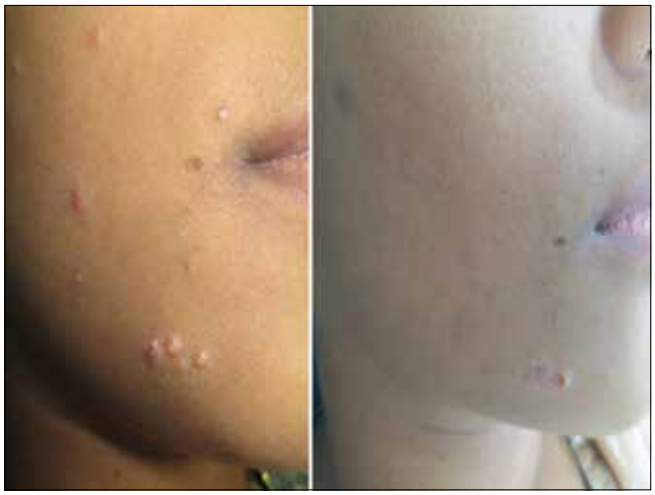

Figure 4: Before and after treatment with imiquimod

Of the 20 patients who received KOH solution, 10 (50%) showed adverse effects, whereas of the 20 patients who received imiquimod, only 4 (20%) showed adverse effects. The result was significant statistically with $P = 0.18$. The most common side effect observed after treatment with KOH was pigmentary disturbances, 6 out of 20 patients showed hypopigmentation, Whereas 4 showed hyperpigmentation and one patient showed ulceration [Figure 8]. Five of these patients also complained of burning sensation. The most common adverse effect seen with imiquimod was erythema, (2 patients). A comparison of adverse effects seen in both the groups was highlighted in Figure 9.

DISCUSSION

The faster onset of action and better efficacy of 10% KOH can be ascribed to its potent tissue destructive ability whereas imiquimod acts by inducing cell mediated immunity, hence the delayed response.[12] This can also explain the continued appearance of new lesions in patients receiving imiquimod and not KOH as the early destruction caused by KOH may prevent autoinoculation.

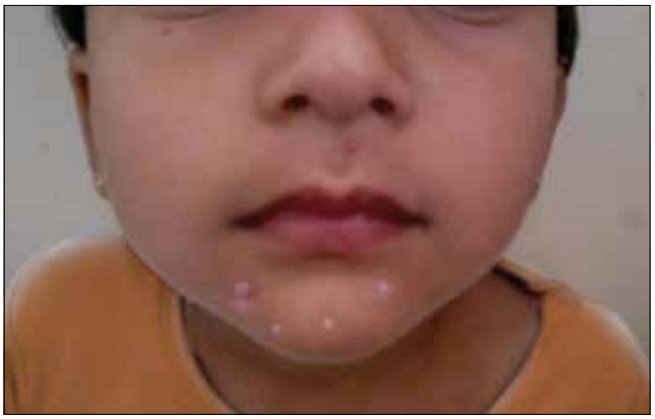

Figure 5: Pretreatment

At the end of 12 weeks, Metkar *et al*. the authors found complete clearance of lesions in 8 (57%) out of 14 patients with imiquimod, and 8 (42.1%) out of 19 patients with KOH. This is in contrast with the finding of our study.[13]

In the study by Seo *et al*., absolute clearance of lesions was seen in 8 (57%) of 14 patients with imiquimod, and 10 (77%) out of 13 patients with KOH, which is in accordance with the sfindings of our study.[14]

Our results however showed a higher rate of complete clearance. This can be attributed to the fact that there was only one giant MC lesion in our study, the remaining being small lesions.

In the study by Mahajan *et al*., 27 patients were asked to apply 20% KOH solution once daily at bedtime. All the children achieved a clearance after a mean period of 17 days.[15]

Puri observed complete clearance of genital MC lesions in 27 (75%) of the 36 patients with once daily application of 5% imiquimod.[16]

Table 1: Comparison of reduction in the lesional counts between the two groups

	Minimum		Maximum		Mean		Median		Mann Whitney test *z* value	*P* value
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B		
No. of lesions-initial	3	3	15	24	7.20	7.10	6.00	6.00	0.72	0.470 Not significant
No. of unchanged lesions- EOW4	1	0	13	12	4.55	2.75	3.50	2.00	2.59	0.010 Significant
No. of unchanged lesions- EOW 8	0	0	10	7	2.30	1.10	2.00	1.00	2.59	0.010 Significant
No. of unchanged lesions- EOW12	0	0	5	2	0.90	0.20	0.50	0.00	2.53	0.019 Significant

EOW: End of Week

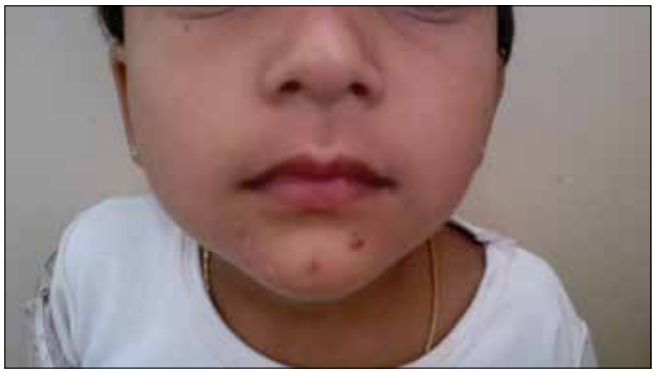

Figure 6: Pigmentary disturbance seen following treatment with potassium hydroxide

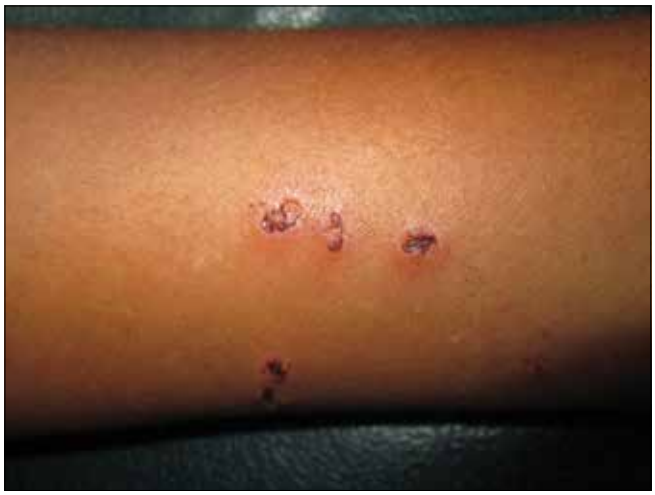

Figure 8: Ulceration following treatment with potassium hydroxide

Figure 7: Before and after treatment with potassium hydroxide

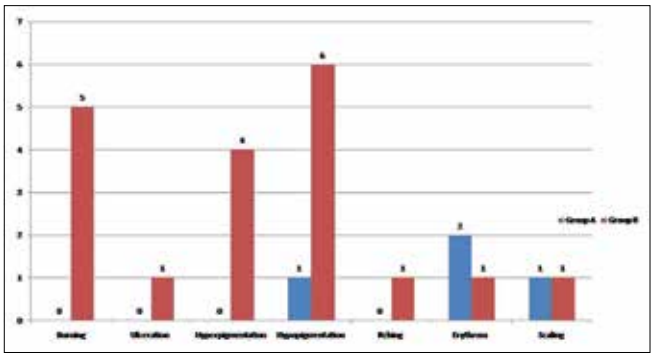

Figure 9: Comparison of adverse effects in both groups

Both the studies indicate that daily application of KOH and imiquimod brings about better efficiency and at a faster rate. The increased concentration also might have a role in faster clearance.

Four (20%) out of 20 patients receiving imiquimod showed adverse effects, with 2 showing erythema, 1 showing scaling and 1 showing hypopigmentation. In the study conducted by Barba *et al*., 6 of the 12 patients had erythema. This may be attributed to the daily application of imiquimod in this study, as opposed to thrice weekly in ours.[17] Mosher and Lio reported febrile seizures and cytokine dermatitis with the use of imiquimod, which we did not come across.[18]

In those who received 10% KOH, 10 (50%) out of 20 patients showed adverse effects, 6 patients showed hyperpigmentation and 4 showed hypopigmentation, 5 of these patients complained of burning. Ulceration with secondary infection, erythema, itching and scaling were seen in one patient each. Parent of the patient who developed ulceration reported

having applied excessive amounts of KOH 10% hoping for a faster recovery. This is refuted by Mahajan *et al*. in whose study it was found that superficial ulceration could not be avoided even with brief careful application of KOH by the parents.[15] In the same study, 2 patients had to discontinue due to severe stinging. This could have occurred due to daily application of 20% KOH in this study in contrast to thrice weekly application of 10% KOH in our study.

Romiti *et al*. did a study on 5% KOH in the treatment of MC and they found that it was tolerated well by children, the findings in the study by Rajouria and co-workers further strengthened this view. Thus, it can deduced that the unfavorable aftermath of KOH can be reduced by using it in a lower concentration.[19,20]

In their comparative study, Seo *et al*. observed adverse effects including erythema, ulceration, scaling and hyperpigmentation in 6 (46%) out of 13 patients in the imiquimod group and 6 (42%) out of 14 patients in the KOH group.[14] Two patients in the imiquimod group and 1 in the KOH group discontinued the treatment because they could not tolerate the local irritation.

In the study conducted by Metkar *et al*., 15 (78.9%) out of 19 on KOH, whereas 10 (55.5%) out of 18 patients on imiquimod developed adverse effects.[13] The most common adverse effects observed were erythema and crusting in both the groups. Systemic side effects of imiquimod were not seen and no patient discontinued the treatment due to adverse effects. This goes hand in hand with the finding in our study.

In our study patient satisfaction was favorable in both the groups.

CONCLUSION

Both 5% imiquimod cream and 10% KOH solution have turned out to be modalities that are safe, efficacious, and easily usable at home. In a resource poor country like ours, curettage would be the best option, but in the case of recurrence of lesions, children may not allow to repeat the procedure owing to pain and fear. In this scenario, judicious application of 10% KOH solution seems to be prudent as it is inexpensive and efficient, albeit with a few minor adverse effects. If the parents can bear the cost without any serious detriment, then 5% imiquimod cream appears to be a better option as its adverse effects are almost negligible. Further studies need to be done with respect to various concentrations of KOH and a standardized mode of delivery of the drug.

What's new: 5% imiquimod cream, which has been used successfully in the treatment of genital warts, has proven its mettle in resolving lesions of MC. KOH solution when used in the concentration of 10% is effective and safe in treating MC.

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