IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 2 Ver. 6 February. (2018), PP 08-15
www.iosrjournals.org

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

Dr Nivedita Devi Vukkadala[1], Dr Ganga Bhavani Mathala[2]
(Department of DVL, Rangaraya medical college, Kakinada, Andhra Pradesh, INDIA)
Corresponding author: Dr Ganga Bhavani Mathala[2]

Abstract :
Background: *Molluscum contagiosum (MC) is a common cutaneous viral infection in children. Active management is preferred to avoid spread and for cosmetic reasons. Many traumatizing treatment modalities are available which are hospital based and evoke panic in children. Hence this study was conducted in the quest of alternate home based painless modality in children.*
Aims and Objectives: *To evaluate and compare the safety and efficacy of 5% imiquimod cream and10% potassium hydroxide (KOH) solution for the treatment of MC in paediatric age group.*
Methods: *The study was conducted from January 2016 to June 2017. 36 Pediatric patients with MC were divided into two groups. 18 Patients were treated with 5% imiquimod cream (Group A) and other 18 were treated with 10% KOH solution (Group B). Patients were followed up on 4^{th}, 8^{th} and 12^{th} week of treatment.*
Results: *At the end of 12 weeks, out of 18 patients who received 10% KOH, 16 patients showed complete clearance, whereas out of 18 patients who received 5% imiquimod, only 11 patients showed total clearance of lesions. In imiquimod group 10 patients had side effects with erythema and hypopigmentation being the most common, while in KOH group 11 patients had side effects, hyperpigmentation being the most common.*
Conclusion: *With only minor adverse effects, 10% KOH is an inexpensive and efficient modality for the treatment of MC. Although 5% imiquimod was effective cosmetically in clearing the lesions with minimal adverse effects, the longer duration required for its action may preclude its wider use.*
Keywords - *5% Imiquimod, Molluscum contagiosum, 10% Potassium hydroxide*

Date of Submission: 02-02-2018 Date of acceptance: 17-02-2018

I. Introduction

Molluscum contagiosum is a common cutaneous viral infection seen in children, caused by molluscum Contagiosum virus which is a large DNA virus, a member of the family Poxviridae and the only member of the genus Molluscipoxvirus. [1] The disease is more prevalent in children (peak incidence between 2 and 5 years) and a later incidence peak in young adults is attributable to sexual transmission with lesions more common in the genital area. [2]

Although it is a self-limiting condition, a decision may be made in favour of active therapy to prevent further spread, relieve symptoms and prevent scarring and for cosmetic and social reasons. [3] Various treatment modalities include first line: cantharidin, trichloroacetic acid, salicylic acid, adapalene, benzoyl peroxide, nitric oxide cream, potassium hydroxide, surgical irritation. The second line modalities include surgical removal and immunomodulators like imiquimod, interferon, and cimetidine. Antiviral agent like cidofovir and intravenous paclitaxel are used as third line drugs. [4] 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 and furthermore, parents do not favour frequent visits to the hospital as children exhibit high levels of anticipatory anxiety. [5]

KOH is a strong alkali, which is known to digest proteins and lipids. It bears a keratolytic property and known to penetrate deeply and destroy the skin. [6] Imiquimod, a member of the imidazoquinoline family, is a potent TLR-7 agonist which induces synthesis and release of several endogenous pro-inflammatory cytokines from Langerhans cells, monocytes/macrophages and dendritic cells. These include IFN-α, TNF-α and IL- 1, 6, 8, 10 and 12, which in turn activate and perpetuate cell-mediated immune responses. [7]

Taking into consideration the above facts the present study has been undertaken to evaluate and compare the efficacies of 5% imiquimod cream and 10% potassium hydroxide (KOH) solution for the treatment of MC in pediatric population.

II. AIMS And OBJECTIVES

To study the efficacy of 5% imiquimod and 10% KOH individually, and to compare the efficacies of both the agents in the treatment of molluscum contagiosum.

III. Materials And Methods

After obtaining permission from institutional ethics committee, this comparative study was conducted over a period of eighteen months from January 2016 to June 2017 in the Department of Dermatology, Venereology and Leprosy, Rangaraya Medical College, Kakinada**.** During this period, thirty six patients of pediatric age group attending the OPD, with clinically diagnosed molluscum contagiosum were recruited to this study. Patients were divided into two groups, eighteen patients were treated with 5% imiquimod cream (group A) and the other eighteen were treated with 10% KOH solutions (group B).

3.1 Inclusion criteria:

1. Presence of minimum of 3 lesions
2. Patients who are willing to undergo the treatment and come for follow up.

3.2 Exclusion Criteria*:*

1. Patients with eyelid involvement.
2. Patients with secondary infection.
3. History of hypersensitivity to imiquimod.

3.3 Method of Study:

Written informed consent was taken. Details of symptoms, duration, family history, site and number of lesions were recorded. Photographs were taken before and after the treatment. The importance of regular attendance was stressed upon to all the patients and their parents to prevent defaulting.

Patients in group A were given 5% imiquimod cream in 0.25g sachets and they were advised to apply a thin layer, rubbing it until it was no longer visible. Patients in group B were given 10% KOH solution with instructions to apply using a cotton swab and to avoid any spillage over normal skin. Both the groups were advised to apply the respective agents at night and wash off in the morning, three times a week for twelve weeks or until the lesions cleared, whichever was early.

Patients were followed up on the 4^{th}, 8^{th} and 12^{th} week of treatment. On each visit, clinical response to treatment, efficacy and tolerability parameters were evaluated. Assessment of response was graded as

1. Complete cure: Disappearance of all lesions in the treatment period (100%)
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 patient.

3.4 INVESTIGATIONS

Complete blood picture, urine analysis and HIV testing were done in all patients.

The results of the study are compiled, tabulated, analyzed and comparison of response between two groups was done using the help of statistician using Chi-square test.

IV. Results

All the 36 patients completed the study. Maximum number of cases were in the age group of 1-10(66.7%). 50% were females and 50% were males in the study. Out of the total number of 36 patients, rural population was 28 (77.8%) and the urban population was 8 (22.2%). 19 (52.8%) Belonged to middle socio economic status and 17(47.2%) were from low socio-economic status. Out of 36 patients, majority 26 (72.2%) had disease duration of less than 3 months, 6 (16.6%) had disease duration of 3-6 months and only 4 (11.1%) had disease duration of more than 6 months. 26 patients (72.2%) had less than 15 lesions, 7(19.4%) had 16-30 lesions, and only 3 (8.3%) had >30 lesions. Most common site of occurrence was the face followed by extremities, trunk and genitalia which were involved in 26, 9, 7 and 3 patients respectively. Multiple sites were involved in 8 patients. Past history of MC was present in 5 (13.8%) patients. One patient was a known case of HIV on HAART therapy with a CD4 count of 152 cells/mm^3. A positive family history was obtained in 13 out of 36 patients (36%). Only 4 patients gave history of atopic dermatitis.

Table 1: Demographic data and Base line clinical data.

Age group	
1-10	66.7 %
11-18	33.3 %
Gender	
Male	50 %
Female	50 %
Geographic area	
Urban	22.2 %
Rural	77.8 %
Socio-Economic Status	
Upper	0 %
Middle	52.8 %
Lower	47.2 %
Occupation	77.8%
Students	22.2%
Others	
Duration of disease	
< 3 months	72.2 %
3-6 months	16.7 %
> 6 months	11.1 %
No of Lesions	
3-15	72 %
16-30	19.4 %
>30	8.3 %
Past History	
Present	13.8 %
Absent	86.2 %
Family History	
Present	36 %
Absent	64 %
Atopic Dermatitis History	
Present	11.1 %
Absent	88.9 %

At the end of this study, in Group A complete cure was seen in 11 (61.1%) out of the 18 patients, with none showing clearance by 4 weeks, 6 patients showing complete clearance by 8 weeks and 5 by 12 weeks. From the remaining 7 patients 3patients had moderate improvement and 4 patients had slight improvement. In Group B complete cure was seen in 16 (88.9%) out of 18 patients, out of which 10 patients were cleared of lesions by 4 weeks, another 5 by the end of 8 weeks and 1 more by the end of 12 weeks. The remaining 2 patient's one had moderate improvement and one had slight improvement. None of the patients from both groups were non responders. 5 (27.7%) from group A, and 2 (11.1%) from group B, got new lesions during the treatment period. The difference was not statistically significant (p= 0.206) (Table.2)

Table 2: Comparison of response in all the patients

	Group A	%	Group B	%
Complete cure (100%)	11	61.1	16	99.1
Moderate improvement (>50%)	3	16.6	1	5.5
Slight improvement (<50%)	4	22.2	1	5.5
No response	0	0	0	0
Relapse	0	0	2	11.1

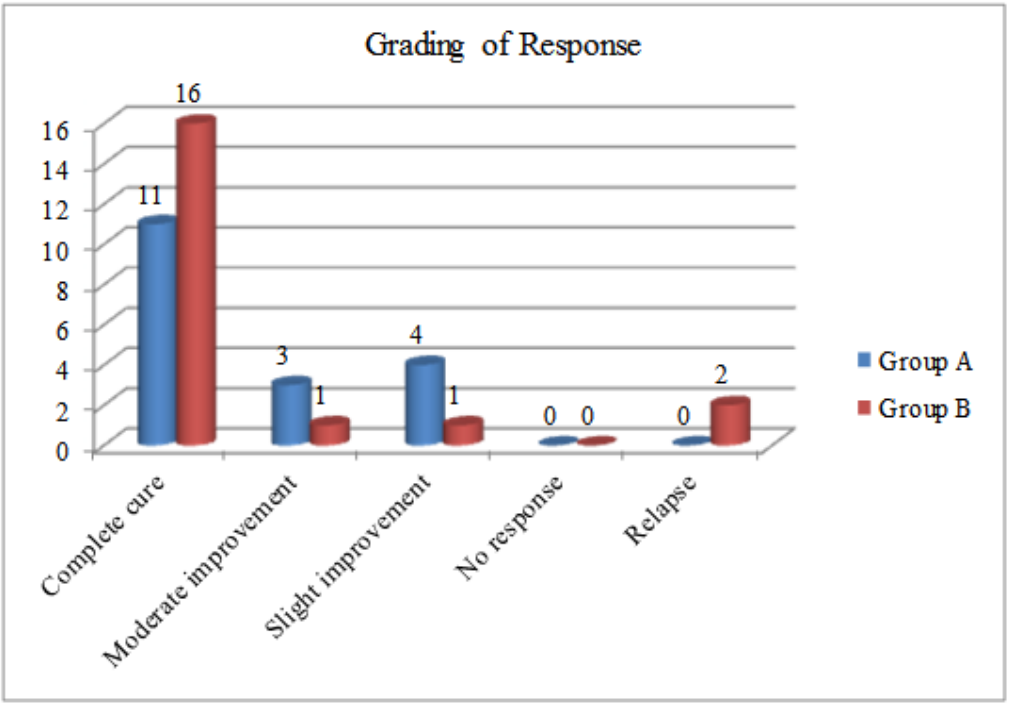

Figure 1: Bar diagram showing grading of response in all patients.

Initial distribution of number of lesions was statistically similar between two groups with *P* = 0.13.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 17.5 ± 13.42 standard deviation (SD) to 4 ± 8.17SD at the end of 12 weeks in patients treated with imiquimod. 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* = 0.009 in Group A patients. The mean lesional count decreased from 10.94 ± 12.01 SD to 0.38 ± 1.42 SD at the end of 12 weeks with 10% KOH solution. This reduction in the number of lesions at the end of 12 weeks was statistically significant *P* = 0.0007 in Group B patients.

Table 3: Comparison of reduction in the lesional counts between the two groups

	No. of lesions (Mean + SD)		P-Value
	Group A	Group B	
Week 0	17.5 ± 13.42	10.94 ± 12.01	0.13
Week 4	11.8 ± 9.73	2.11 ± 3.10	0.0003
Week 8	7.16 ± 9.39	0.5 ± 1.69	0.0055
Week 12	4 ± 8.17	0.38 ± 1.42	0.0727

On comparing the lesional count (Mean + SD) in both groups at follow up period the p-value was 0.0003 at the end of 4th week which was statistically significant. At the end of 8th week the p-value was 0.0055 which was also significant. At the end of 12th week no significant difference was observed between the two groups as in previous follow-ups with a p=value of 0.0727[Table3].

Out of 18 patients in each group, 10 (55.5%) in Group A had side-effects, and 11 (61.1%) in group B had side-effects. The difference was statistically not significant (p=0.73). Out of 10 cases with side effects in group A, 5(27.7%) had erythema and hypopigmentation, followed by hyperpigmentation in 3 (16.7%), 1 (5.6%) had erosions, and 2 (11.1%) had scaling. None had burning and itching. In group B, out of 11(61.1%), 8 patients (36.7%) had hyperpigmentation, followed by burning sensation in 3(16.7%) and erythema, ulceration, itching, hypopigmentation and secondary infection in 1 (5.6%) patient[Figure2].

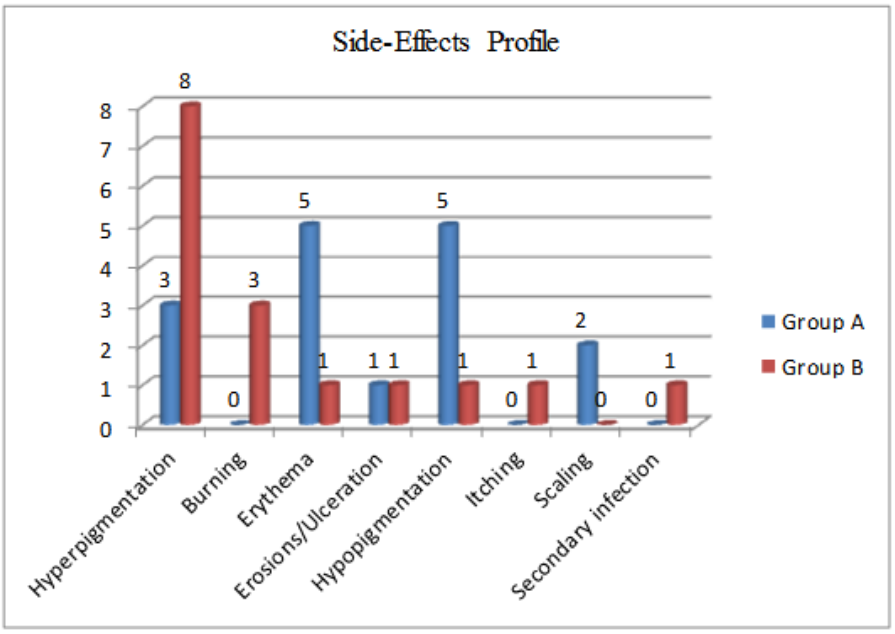

Figure 2: Bar diagram showing side-effects profile.

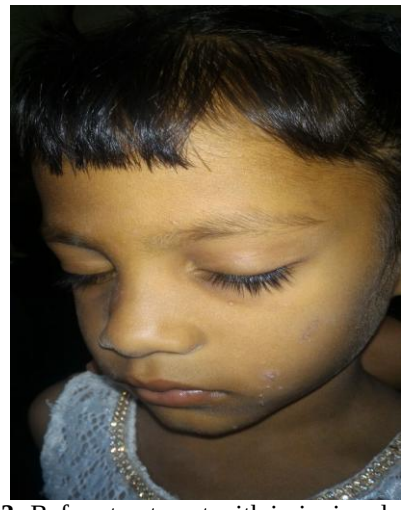

Figure 3: Before treatment with imiquimod

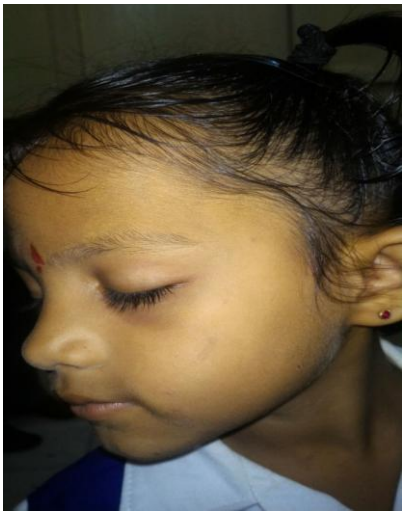

Figure 4:complete cure with imiquimod at WK 12

Figure 5:Erythema and scaling following Imiquimod

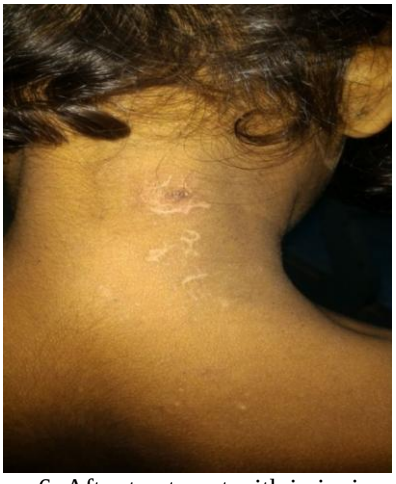

Figure 6: After treatment with imiquimod at week 12 (pigmentary disturbances).

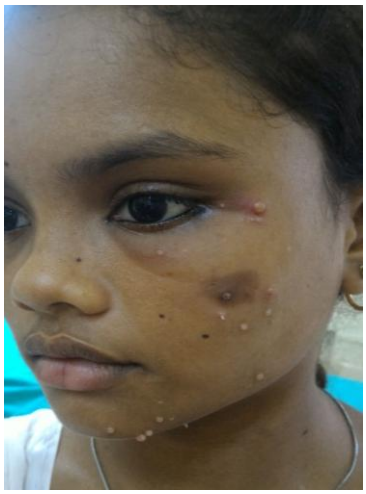

Figure 7:Before Treatment

Figure 8:After treatment with KOH at 4th week (hyperpigmentation)

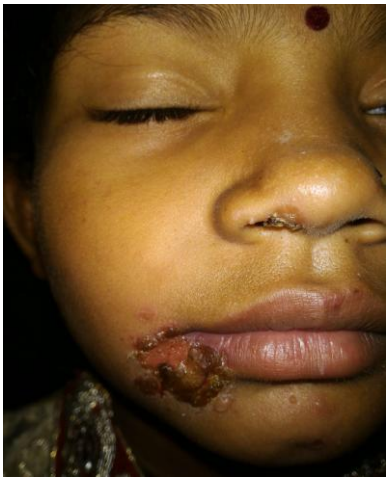

Figure 9: Ulceration & secondary infection following treatment with KOH.

Figure 10: Complete clearance of ulcer without sequelae.

V. Discussion

Despite many options, no single therapy was FDA approved for treatment of MC, which was safe and can be used at home. [5] Taking this into consideration, this randomized controlled study was undertaken to assess and compare the efficacies of 5% imiquimod cream and 10% KOH aqueous solution for the treatment of MC. KOH acts by dissolving the keratin and destroying the skin and hence it has rapid onset of action whereas imiquimod is a tissue response modifier that induces IFN-α, a potent antiviral agent thus stimulating cell mediated immunity and hence delayed response. [9] This can also explain the higher incidence of continued appearance of new lesions in patients receiving imiquimod and lesser number in KOH as the early destruction caused by KOH may prevent autoinoculation and disease spread. [5] Relapses were nil in imiquimod group compared to KOH group which can be attributed to its immunomodulatory action. Due to slow onset of action many patients may discontinue the treatment with imiquimod so patient's education regarding its mode of action and response is very important for their adherence to the treatment.

Most common site of occurrence of lesions in children was the face followed by extremities, trunk which were involved in 26(72.2%), 9(25%), 7(19.4%) and patients which was similar to the study by Muzaffar et al in which 25 (75.7%) had lesions on the face, 15 (45.4%) on limbs, 13 (39.4%) on trunk respectively. [10]

The minimum duration of infection was 10 days, and maximum duration was 1 year with a mean duration of 3.2 months with majority 72.2% had disease duration of less than 3 months. In a study conducted by Metkar et al maximum number of cases had disease duration less than 3months, and the minimum duration of infection was 15 days, and maximum duration was 1 year which was similar to the present study. [11]

Four of the patients in the present study complained of pruritus unlike in the study by Seo et al, where 15 of the 30 patients had pruritus. No one had eczematous dermatitis. [9]

In the present study one case was a known HIV patient on HAART therapy who showed only moderate response to 5%imiquimod cream.

Out of 36 patients, 4(11.1%) patients gave history of atopy, this was similar to the findings of Metkar et al study in which 4 out of 40 patients had history of atopy and chathra et al study in which 3 out of 40 patients had history of atopy. In the present study, positive family history was obtained in 13(36.1%) of the total patients, whereas in the study by chathra et al, history of similar complaints in the family was noted in 18 cases out of the total 40 cases which was similar to the present study, where as in Metkar et al, study positive family history was noted only in 8 cases out of 40 cases which is in in contrast to present study. [5, 11]

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, and Chathra et al observed absolute clearance of lesions in 10 (50%) of 20 patients with imiquimod and 17 (85%) out of 20 patients respectively which were more in accordance with findings of the present study.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. [5, 9,11]

In the study conducted by Mahajan *et al*, 27 patients were asked to apply 20% KOH solution once daily at bedtime and all the children achieved a clearance after a mean period of 17 days. In another study by Puri complete clearance of genital MC lesions was seen in 27 (75%) of the 36 patients with once daily application of 5% imiquimod.Both the above 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 the speedy clearance. [12, 13]

In a study conducted by Metkar et al, 15(78.9%) out of 19 on KOH developed side effects, whereas 10(55.5%) out of 18 patients on imiquimod developed side effects which were similar to the present study. The commonest side-effects observed by them were erythema and crusting in both the groups whereas hyper pigmentation, erythema and hypopigmentation were observed in our study. [9]In their comparative study, Seo et al observed side-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. In her study Chathra et al observed side effects in 10 (50%) out of 20 patients who received KOH solution, whereas of the 20 patients who received imiquimod, only 4 (20%) showed adverse effects which were in contrast to the present study. [5,9]

Romiti et al. reported a study in which patients were instructed to apply 5% KOH solution twice a day. This was done in an attempt to reduce the side effects observed with higher concentration. They found 5% KOH as effective and less irritating when compared to 10% KOH. [14]

No serious systemic side-effects and local side-effects like scarring were observed in present and all the adverse effects were mild and transient and tolerable. Patient's satisfaction was good in both groups.

VI. Conclusion

In conclusion, both 5% imiquimod cream and 10% KOH solution have turned out to be modalities that are safe, efficacious and easily usable at home. They have an advantage over curettage because they are less traumatic, less painful, and easier to administer with high patient compliance especially in pediatric age group KOH seems more effective in clearing the lesions, with a faster rate of response. On the other hand, imiquimod was cosmetically superior to KOH as pigmentary disturbances were commonly observed with KOH. However, KOH proved to be superior over imiquimod due to its cost effectiveness and faster onset of action.

References

[1]. John M. Douglas, Molluscum Contagiosum, in King K Holmes, P.Frederick Sparling, Walter E.Stamm, Peter Piot, Judith N.Wasserheit, Lawrence Corey (Ed), Sexually Transmitted Diseases, 4th ed. (The McGraw-Hill Companies; 2008)

[2]. Nameer K, Al-Sudany a, Dler R.Abdulkareem, A comparative study of topical 10% KOH solution and topical 25% podophyllin solution as home-based treatment of molluscum contagiosum. Journal of Dermatology & Dermatologic Surgery 2016; 20: p. 107–114.

[3]. van der Wouden JC, van der Sande R, van Suijlekom, Smit LW, Berger M, Butler. Interventions for cutaneous molluscum contagiosum. Cochrane Database Syst Rev. 2013 aug 8; 7(4).

[4]. Sterling JC, Virus Infections, in. Christopher E. M. Griffiths., Jonathan Barker, Tanya Bleiker, Robert Chalmers, Daniel Creamer (Ed), Rook's Textbook of Dermatology. 9th ed, (wiley and blackwell; 2016)

[5]. Chathra N, Sukumar D, Bhat RM, Kishore BN. A comparative study of 10% KOH solution and 5% imiquimod cream for the treatment of Molluscum contagiosum in the pediatric age group. Indian Dermatol Online J. 2015; 6(2): p. 75–80

[6]. Sequeira FF, Bala NK, Hundi GK, Martis J. A study on the effi cacy of topical 10% potassium hydroxide in the treatment of Molluscum contagiosum. Muller J Med Sci Res. 2016; 7: p. 1-3.

[7]. Lacarrubba F, Nasca MR, Micali G. Advances in the use of topical imiquimod to treat dermatologic disorders. Therapeutics and Clinical Risk Management. 2008; 4(1): p. 87-97.

[8]. Nguyen, Harrison P, Eric Franz, Kelly R. Stiegel, Sylvia Hsu, StephenK.Tyring. Treatment of Molluscum Contagiosum in Adult, Pediatric,and Immunodeficient Populations. Journal of Cutaneous Medicine and Surgery. 2013; 17: p. pp 000–000.

[9]. Seo SH, Chin HW, Jeong DW, Sung H. An open randomized, comparative clinical and histological study of imiquimod 5% cream versus 10% potassium. Ann Dermatol. 2010; 22(2): p. 156-162.

[10]. Farhana Muzaffar, Farzana Faiz. Comparison of 5% potassium hydroxide with 10% potassium hydroxide solution in treatment of molluscum contagiosum: A comparative study. Pakistan Association of Dermatologists. 2014; 24(4): p. 337-341.

[11]. Metkar A, Pande S, Khopkar U. An open, nonrandomized, comparative study of imiquimod 5% cream versus 10% potassium hydroxide solutionin the treatment of Molluscum contagiosum. Indian J Dermatol Venereol Leprol. 2008; 74: p. 614-8.

[12]. Mahajan BB, Pall A, Gupta RR. Topical 20% KOH – An effective therapeutic modality for Molluscum contagiosum in children. Indian J Dermatol Venereol Leprol. 2003; 69: p. 175-7.
[13]. Puri N. A study on the use of imiquimod for the treatment of genital molluscum contagiosum and genital warts in female patients. Indian J Sex Transm Dis. 2009; 30(2): p. 84-88.
[14]. Romiti R, Ribeiro AP, Grinblat BM, Rivitti EA, Romiti N. Treatment of Molluscum contagiosum with potassium hydroxide: A clinical approach in 35 children. Pediatr Dermatol. 1999; 16: p. 228-31.

DR Nivedita Devi Vukkadala "A comparative study of 5%imiquimod cream and 10% KOH solution for the treatment of Molluscum contagiosum in the paediatric age group" IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) , vol. 17, no. 2, 2018, pp. 08-15.