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EFFICACY OF RANITIDINE IN TREATMENT OF MOLLUSCUM CONTAGIOSUM IN CHILDREN OF LESS THAN 5 YEARS

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ABSTRACT **Background/Aim:** Molluscum contagiousum is a contagious skin disease that primarily affects children in early years of life. The present study intended to evaluate the efficacy of ranitidine in treatment of molluscum contagiousum in children of less than 5 years. **Methods:** A total of 50 children aged <5 years with clinical diagnosis of molluscum contagiosum were enrolled in the study. Chief presenting complaint, duration of complaints, number and site of lesions were noted. Oral ranitidine was started in dose of 5 mg/kg/day in two divided doses for 8 weeks. Follow-up was done after 2, 4 and 8 weeks. Treatment response was assessed in terms of complete response, marked response, moderate response and inadequate response respectively. Post-treatment follow-up was done at 3 and 6 months to assess recurrence. **Results:** Mean age of patients was 24.78±8.81 months (range 18-55 months). Majority (68%) were males. Mean duration of complaints was 3.14 months and mean number of lesions was 17.34. Face/forehead was the most commonly involved site (42%). Cosmetic reasons were the most common complaints (40%). At 8 weeks, 58% patients had complete response, 10 (20%) had marked response, 4 (8%) had moderate response and 7 (14%) had inadequate response. At 6 months, 5 (10%) cases showed recurrence. Inability to achieve complete response was significantly associated with female sex (p=0.044). **Conclusion:** Oral ranitidine was useful in treatment of molluscum contagiosum among young children; however, post-treatment preventive measures are essential to check the recurrence.

KEYWORDS : Molluscum contagiosum, young children, complete response, oral ranitidine.

INTRODUCTION

Molluscum contagiosum is a contagious skin disorder that primarily affects the children. It is usually asymptomatic but sometimes it is accompanied by pain, pruritus, erythema and bacterial superinfection[1]. It is a viral disorder that affects the skin and mucous membranes and is manifested as single or multiple, flesh-colored papules[2]. The causative organism is molluscum contagiosum virus (MCV), which is a virus of the Poxviridae family. The transmission of MCV takes place by direct contact with infected skin[3]. Treatment modalities include mechanical, chemical, immunomodulatory and antiviral modalities[4].

Mechanical treatment includes cryotherapy, curettage, topical povidone iodine and pulse dye laser therapy. Chemical modalities include Cantharidin, potassium hydroxide, podophyllotoxin, trichloroacetic acid, salicylic acid, lactic acid, glycolic acid, benzoyl peroxide, and tretinoin applications. Immunomodulatory treatment includes imiquimod, cimetidine, interferon alfa, candidin, and diphencyprone. Among antivirals, use of cidofovir is quite common[3].

Ranitidine is a histamine receptor antagonist similar to Cimetidine and have a clinically significant immunomodulatory effect[5]. Ranitidine at a dose of 5 mg/kg/day in two divided doses has been reported to be an effective alternative for widespread molluscum in immunocompetent children. Ranitidine exerts an immunostimulatory effect through enhancement of cluster of differentiation 4 (CD4) lymphocytes and suppressing the CD8 lymphocytes. It is also supposed to increase the activity of natural killer, lymphokine-activated killer cells and interferon activated killer cells. Ranitidine may exert its antiviral effects, by increasing the activity of these cells[6]. Some recent studies have also evaluated its clinical efficacy in management of molluscum contagiosum and warts in children without any adverse event[6,7,8]. Encouraged by these studies, we planned this prospective interventional study to assess the efficacy of ranitidine in management of molluscum contagiosum in children aged less than five years.

MATERIAL AND METHOD

This prospective interventional study was carried out among clinically diagnosed patients of molluscum contangiosum aged <5 years attending the Dermatology OPD at Era's Lucknow Medical College & Hospital, Lucknow, for a period of 1 year. Approval for the study was obtained from Institutional Ethics Committee and informed consent was obtained from the parents of participating patients. Those with a history of previous treatment, having any underlying systemic condition or malnutrition, those failing to provide response to treatment at scheduled follow-up and those having less than 90% compliance to treatment were excluded from the study.

Following enrolment in the study, the demographic profile (age, gender) of child was noted, nature and duration of chief complaint was noted. A thorough clinical examination was performed that included counting of number of lesions, site and extent of lesions. Photographic record was made through a digital photograph.

All the patients were then put on oral ranitidine syrup at a dose of 5mg/kg/day in two divided doses for 8 weeks. A compliance sheet was given to caregivers of all the children to note the compliance. During treatment follow-ups were made at 2, 4 and 8 weeks intervals either in person or through a video-conferencing with a high-resolution photograph of the affected site at that time. At every follow-up visit, change in number and size of lesions was noted. The response to treatment was graded as follows:
Complete response 100% resolution,
Marked response 75-99% resolution,
Moderate response 50-75% resolution
Inadequate response resolution

The treatment response was evaluated by comparing the pre-treatment photograph of affected site with the follow-up photograph of the affected site by two residents. In case of a disagreement between two, the final assessment, was made by the senior consultant.

All the patients were then followed up in person or telephonically at 3 and 6 months' intervals. Recurrence, if any was noted.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 21.0. Data has been presented as mean±SD and numbers and percentages. Chi-square and Independent samples 't'-tests were used to compare the data. A 'p' value less than 0.05 were considered to be significant statistically.

RESULTS

Age of children ranged from 18 to 55 months. Mean age of children was 24.78±8.81 months. Majority of children were males (68%). There were 16 (32%) females. Duration of complaints ranged from 15 days to 6 months with a mean of 3.14±1.59 months. Number of lesions ranged from 8 to 25 with a mean number of 17.34±5.39. Face/forehead was the most commonly involved site (42%) followed

by neck (14%), trunk and forearm (12% each), back (8%), groin and legs (6% each) respectively. Maximum numbers of children were asymptomatic and visited us for cosmetic reasons; a total of 19 (38%) had pain while 11 (22%) had pruritis (Table 1).

At first follow-up (2 weeks after start of treatment), a total of 4 (8%) had complete response, 2 (4%) had marked response, 14 (28%) had moderate response while majority (n=30; 60%) had inadequate response. At second follow-up (4 weeks after start of treatment), a total of 12 (24%) had complete response, 11 (22%) had marked response, 18 (36%) had moderate response and 9 (18%) had inadequate response. At third and final follow-up (8 weeks after start of treatment), a total of 29 (58%) had complete response, 10 (20%) had marked response, 4 (8%) had moderate response and 7 (14%) had inadequate response. Thus complete resolution of lesions was seen in 29 (58%) cases at the end of treatment, while 14 (28%) showed marked to moderate response and only 7 (14%) had inadequate response (Table 2).

At 3 months follow-up, none of the patients showed a recurrence. However, at six months follow-up, a total of 5 (10%) patients showed recurrence (Table 3).

On evaluating the factors affecting complete response, no significant association of age, duration of complaints, number of lesions, site involved and chief complaints was observed with complete response (p>0.05). However, those with complete response had significantly higher proportion of males (79.3%) as compared to those not having complete response (52.4%) (p=0.044) (Table 4).

DISCUSSION

The present study showed a promising role of oral ranitidine therapy among young children (<5 years old) with molluscum contangiosum. In present study complete to marked response following 8 week of therapy was seen in 78% of children. Moreover, the results seem to be consistent with recurrence observed in only 5 (10%) cases during 6 months of follow-up. The response to treatment was independent of clinical and demographic profile of patients except for sex-related differences with a better rate of complete response in males as compared to that in females. In present study, complete response within 2 and 4 weeks was observed in 8% and 24% patients. By 8th week, as many as 58% patients showed complete response.

Ranitidine is a histamine receptor antagonist having immunomodulatory effect similar to Cimetidine[5]. It acts by modulation of CD4 and CD8 lymphocytes and promotes the activity of natural killer, lymphokine-active killer cells and interferon activated killer cells that give a boost to cellular immunity and thus accomplish an antiviral status[6]. Despite these wonderful characteristics, the clinical application of Ranitidine for treatment of Molluscum contagiosum is not widely reported. In a recent study, Agarwal *et al.*[7] reported a series of 24 children aged 1.5 to 11 years who were put on oral ranitidine therapy for 8 weeks as in present study. In their series, they also started witnessing complete resolution of lesions by second week interval itself (1/24; 4.2%). By eighth week, they reported complete resolution in 14/19 (73.7%) patients that could be followed up while 1 patient showed a decrease in size and 4/19 (21.1%) showed no change. Thus treatment inadequacy rate was 21.1% in their study as compared to 14% in present study. A better outcome in present study could be attributable to two factors – firstly we provided the patients with a compliance sheet that helped to ensure a better compliance. Secondly, we included only those patients in our study who attended all the follow-up intervals and who had a compliance rate >90%. Incidentally, owing to spread of pandemic, we had to resort to video-conferencing to ensure follow-up of patients at scheduled interval, however, probably pandemic situation was a motivating factor to ensure better treatment compliance. In another case study, Chitalia *et al.* [6] also reported complete resolution of molluscum contangiosum lesion in an 8-year-old boy within 6 weeks of oral ranitidine treatment. In present study, non-responsiveness to treatment was found to be significantly associated with female sex. In the study by Agarwal *et al.*[7] too, out of four non-responders, three were females. Sonthalia *et al.*[9] reported two cases of molluscum contangiosum who were tried for intralesional vitamin D immunotherapy. Of this one case was a girl with a failed treatment response to oral ranitidine. This sex- specific response to ranitidine for treatment of molluscum contangiosum has not been reported to be of statistical significance elsewhere. However, in an animal study[10], the bioavailability of oral ranitidine was shown to be affected by gender with female rats showing an impaired bioavailability of ranitidine following oral intake of the drug. Whether the findings in present study are incidental or show a sex-related bioavailability difference in ranitidine remains to be explored further.

As far as recurrence is concerned, it was observed to be 10% in present study which is similar to 2/19 (10.5%) cases as reported by Agarwal *et al.*[7] in their study. One of the reasons for recurrence could be continued skin-to-skin transmission risk among these children. The findings suggest that Ranitidine treatment should also be accompanied by preventive measures to reduce risk exposure.

In present study, we did not note any reported adverse effect of ranitidine, such as headache, constipation, diarrhea, nausea and vomiting in any of our cases. No such side effect of ranitidine was also reported in the earlier studies too[6,7]. The reason for this could be the use of a relatively much lower dose of ranitidine in present study. In literature, use of 75 mg Ranitidine dose given to children has also been reported to be effective and free of any major side effect[11].

The findings of present study thus show that Ranitidine is effective in managing molluscum contangiosum in young children aged below five years. One of the limitations of present study was absence of a comparative group, further studies with inclusion of a comparative group should also be performed in order to assess the relative efficacy of ranitidine as compared to other alternatives.

CONCLUSION

The present study showed a complete to marked response rate of 78% in young children (<5 years of age) with molluscum contagiosum with a very low recurrence rate. During six months of follow-up there was a recurrence rate of 10%, which suggests the need to adopt preventive measures to avoid recurrence.

Table 1: Demographic and Clinical Profile of patients enrolled in the study (N=50)

SN	Characteristic	Statistic
1.	Mean age±SD (Range) in months	24.78±8.81 (18-55)
2.	Sex Male Female	34 (68%) 16 (32%)
3.	Mean duration of complaints±SD (Range) in months	3.14±1.59 (0.5-6)
4.	Mean number of lesions±SD (Range)	17.34±5.39 (8-25)
5.	Site of lesion	
	Face/forehead	21 (42%)
	Neck	7 (14%)
	Trunk	6 (12%)
	Forearm	6 (12%)
	Back	4 (8%)
	Groin	3 (6%)
	Legs	3 (6%)
6.	Chief presenting complaint	
	Asymptomatic/Cosmetic	20 (40%)
	Pain	19 (38%)
	Pruritis	11 (22%)

Table 2: Pattern of response to treatment

SN	Time of follow-up	Response			
		Complete	Marked	Moderate	Inadequate
1.	First follow-up (2 weeks)	4 (8%)	2 (4%)	14 (28%)	30 (60%)
2.	Second follow-up (4 weeks)	12 (24%)	11 (22%)	18 (36%)	9 (18%)
3.	Third follow-up (8 weeks)	29 (58%)	10 (20.0%)	4 (8%)	7 (14%)

Table 3: Follow-up for Recurrence

Follow up interval	No. of cases showing recurrence	% of cases showing recurrence
3 months	0	0
6 months	5	10%

Table 4: Factors affecting outcome

SN	Characteristic	Resolved (n=29)	Not resolved (n=21)	Statistical significance
1.	Mean age±SD (months)	23.93±8.99	25.95±8.62	t=0.798; p=0.429

2.	Sex Male Female	 23 (79.3%) 6 (20.7%)	 11 (52.4%) 10 (47.6%)	 2=4.059; p=0.044
3.	Mean Duration of complaints (months)	3.29±1.59	2.93±1.60	t=0.798; p=0.429
4.	Mean number of lesions±SD	16.52±5.38	18.48±5.32	t=1.277; p=0.208
5.	Site			
	Face/forehead	11 (37.9%)	10 (47.6%)	2=11.002; p=0.088
	Neck	5 (17.2%)	2 (9.5%)	
	Trunk	4 (13.8%)	2 (9.5%)	
	Forearm	5 (17.2%)	1 (4.8%)	
	Back	0	4 (19.0%)	
	Groin	3 (10.3%)	0	
	Legs	1 (3.4%)	2 (9.5%)	
6.	Chief complaints			
	Asymptomatic/Cosmetic	11 (37.9%)	9 (42.9%)	2=1.632; p=0.442
	Pain	13 (44.8%)	6 (28.6%)	
	Pruritis	5 (17.2%)	6 (28.6%)	

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