Ingenol mebutate gel for the treatment of molluscum contagiosum: An open-label comaparative pilot study

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Title page

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(**Running head**: Ingenol mebutate for molluscum contagiosum)

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To the Editor:

Molluscum contagiosum (MC) is a common contagious cutaneous viral disease caused by the MC virus. Although MC resolves spontaneously, the demand exists for a rapid, less painful, and safe treatment due to their contagious nature, pruritus, cosmesis, and pain.[1]

Recently, ingenol mebutate gel has been approved for the treatment of actinic keratosis by inducing direct and rapid cell death and immune responses.[2] Although ingenol mebutate has the potential for the treatment of other cutaneous diseases, there has been a single case report of MC treated with ingenol mebutate in English literature.[3]

Our aim was to perform a pilot study of ingenol mebutate gel for patients with MC lesions. Institutional review board approval was provided by the Ethics Committee of Pusan National University Hospital (H-1902-005-076). A total of 19 patients with MC lesions were enrolled in the dermatology department of Pusan National University Hospitals (Busan and Yangsan) from 2015 to 2017. 10 and 9 patients were randomly assigned to the ingenol mebute group and imiquimod group, respectively. In ingenol mebutate group, 0.015% ingenol mebutate gel was applied to the top of the lesion once daily for 3 consecutive days per week. In imiquimod group, 5% imiquimod cream was applied directly on the lesion once daily for 5 times per week. They were applied until the lesions disappear completely.

We observed significantly reduced MC lesions all throughout the follow-up period in ingenol mebutate group, but at week 2, there was no significant decrease of lesions in imiquimod group (Table I). Compare to imiquimod group, ingenol mebutate group showed significantly less number of lesions at week 2, week 4, week 8 and week 12. Complete clearance rate of ingenol mebutate group (90.0%) was higher than the rate of imiquimod group (33.3%) at week 12. Furthermore, it takes significantly less time to complete clearance and perilesional erythema in ingenol mebutate group compare to imiquimod group.

Representative clinical course of MC following ingenol mebutate application was presented on Supplemental Figure 1. Crusts on MC lesions were more frequently observed in ingenol mebutate group (9 of 10) compare to imiquimod group (3 of 9) (*P = .017*), however rate of other local and systemic adverse events including pain (10.0% for ingenol mebutate group and 11.1% for imiquimod group) and pruritus (50% for ingenol mebutate group and 44.4% for imiquimod group) were not different between both groups, and these were tolerable in all patients.

The major limitations of this study were the fact that it was unblinded study with small sample size and lack of explicit placebo group or active comparator group, though imiquimod could be considered a placebo arm in this study, as it has recently been demonstrated not to be effective for MC.[4] In summary, our findings suggest that ingenol mebutate could shorten the period of autoinoculation and transmission by rapid clearance of MC lesions. Destructive treatments such as cryotherapy or curettage are also rapid but may cause pain or not be well tolerated by children. Larger, controlled studies of ingenol mebutate for MC are warranted.

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81 **Table I.** Demographics and treatment outcomes of the subjects

Characteristics	Ingenol mebutate (n=10)	Imiquimod (n=9)	*P* value
Age, y, mean (range)[#]	5.6 (1.7-8.0)	4.3 (1.7-8.0)	.173
Male, n (%)[†]	4 (40.0)	5 (55.6)	.414
Duration, m, mean (range)[#]	8.5 (2.0-24.0)	6.4 (2.0-24.0)	.453
Location, mean (range)[#]			
Face	11.2 (0-36)	4.6 (0-25)	.218
Trunk	12.0 (0-35)	5.3 (0-24)	.321
Extremities	12.6 (0-55)	4.8 (0-28)	.063
Groin	1.3 (0-11)	13.6 (0-57)	.216
Number of the lesions, mean (range)[#]			
Week 0	37.1 (11-90)	28.2 (7-85)	.205
Week 2	9.6 (0-42)	20.9 (6-55)	**.030**[*]
Week 4	6.6 (0-42)	17.9 (2-48)	**.022**[*]
Week 8	5.3 (0-41)	12.6 (0-26)	**.022**[*]
Week 12	3.6 (0-32)	7.7 (0-25)	**.035**[*]
Complete clearance, n (%)[†]			
Week 2	1 (10.0)	0 (0.0)	.526
Week 4	4 (40.0)	0 (0.0)	.054
Week 8	7 (70.0)	1 (11.1)	**.010**[*]
Week 12	9 (90.0)	3 (33.3)	**.017**[*]
Time to perilesional erythema, weeks, mean (range)[#]	1.1 (0.7-2.0)	2.6 (2.0-4.0)	**.045**[*]
Time to complete clearance, weeks, mean (range)[#]	6.8 (2.0-12.0)	10.8 (8.0-12.0)	**< .001**[*]

82 [#] Mann-Whitney test was done

83 [†] Fisher′s exact test was done

84 [*] Statistical significance was defined as a *P* value less than .05.

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Fig 1. Serial changes of MC lesions following 0.015% ingenol mebutate gel application in a 4-year-old girl at baseline (**A**) and after 1 (**B**), 3 (**C**), and 12 (**D**) weeks.