

## A Multicenter Randomized, Double-Blind, Split-Side, Comparative Study of Moisturizer Containing MAS064D and 1% Hydrocortisone Cream in the Treatment of Infantile Seborrheic Dermatitis

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### Abstract

**Background:** Infantile seborrheic dermatitis (ISD) is a chronic self-limiting disease presenting with erythema, greasy, scaly, or crusting plaque in infants. Many treatments are recommended for treatment of ISD.

**Objective:** To compare the efficacy of moisturizer containing MAS064D and 1% hydrocortisone cream for treatment of ISD.

**Methods:** This study was a multicenter, randomized, double-blind, split-side, comparative study performed at 4 centers. Pediatric patients aged 2 weeks to 12 months, with bilaterally symmetrical distribution of mild to moderate ISD were recruited. Subjects were randomized for treatment with either moisturizer containing MAS064D or 1% hydrocortisone cream on the opposite side of the body (left or right) twice daily, by sequentially numbered bottle from block randomization prior to beginning the study. All investigators utilized standardize scoring to assess patient severity. Lesions on each side were evaluated on day 0, 6-7, 14 and 28.

**Results:** A total of 50 patients were recruited. Both moisturizer containing MAS064D and 1% hydrocortisone cream were effective in the treatment of ISD since day 6-7 with a p-value<0.001. There was no significant difference between both treatments. Adverse events occurred in 2 patients who reported on the side decoded as moisturizer containing MAS064D treatment. One patient (2%) had transient erythema which spontaneously resolved in 30 minutes on the first day after application, and the other patient (2%) had miliaria. There was no report of adverse events on the side that applied 1% hydrocortisone cream.

**Conclusion:** Both moisturizer containing MAS064D and 1% hydrocortisone cream were effective in the treatment of ISD.

**Keywords:** MAS064D; Hydrocortisone; Infantile seborrheic dermatitis; Treatment

### Introduction

Infantile seborrheic dermatitis (ISD) is a chronic self-limited disease that presents with erythema, greasy, scaly, or crusting plaque in infants. Skin lesions usually occur on areas with high concentration of sebaceous glands, on the scalp, face, eyebrow, retroauricular areas and some cases also have skin lesion on the intertriginous areas. ISD presents in the first 2-8 weeks, and persists for 6 to 12 months. Mild cases usually resolve at the age of 8 to 12 months [1]. Data from studies in many countries show that incidence in the first two years of life is 18 to 44.5% [2,3], incidence in Thailand is 13% [4].

The etiology of ISD remains unknown. Increased activity of the sebaceous glands in the newborn from maternal androgen and *Malassezia spp.* may associate with ISD. During the first few months of life, infants often have increased sebaceous secretion and after 6

months the sebaceous secretion diminishes and the clinical of ISD subside. *Malassezia spp.* is thought to activate immune response rather than a simple infection [5]. At present, many studies that have indicated *Malassezia spp.* to play an important role in this condition, even normal numbers of *Malassezia spp.*, can stimulate an inflammatory reaction [6].

There are several effective therapies for ISD including topical corticosteroids, ketoconazole shampoo [7], ketoconazole cream [8,9] and licochalcone [10]. MAS064D, is a moisturizer containing isohexadecane, shea butter, bisabolol and piroctone olamine, which has anti-inflammatory, and antifungal activity [11]. Clinical studies on the use of moisturizing products containing MAS064D in adults have been shown to be effective [11-13]. No or less adverse effects such as slight signs of irritation, rash, itching and stinging sensation have been reported in some patients. The use of moisturizing products containing MAS064D to treat ISD has been shown to reduce erythema, crusting, and oiliness as effective as placebo, but reduction in scaling was more

effective than placebo [14]. The aim of this study was to compare the efficacy of moisturizer containing MAS064D and 1% hydrocortisone cream for the treatment of ISD.

## Methods

Approval for this study was obtained from the Ethics Committee of each center. Written informed consent for participation in the study was provided by parents of all children.

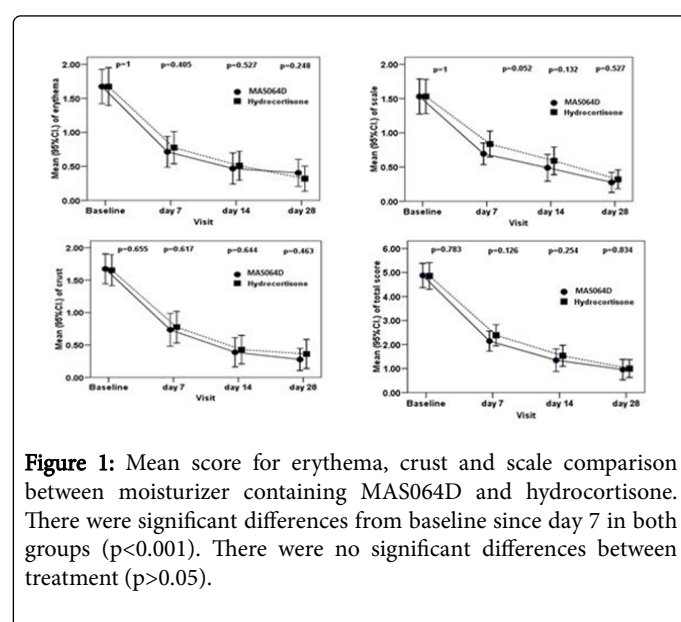
## Study design

This study was a multicenter randomized, double-blind, split-side, comparative study to decrease interpersonal variation of disease severity and response to treatment. We recruited ISD patients from 4 centers and all investigators utilized a standardized scoring system to decrease interpersonal variation of assessment.

## Sample size calculation

This study is a repeated measures design which calculates sample size by formulation of Frison and Pocock (1992) [15]. The statistical significance and power is defined at 0.05 and 0.80, respectively, where  $f(\alpha, \beta) = (Z\alpha/2 + Z\beta)$  [2] and the formulation to determine sample size is shown below:

$$n = \frac{2\sigma^2}{\delta^2} \left[ \frac{1 + (r-1) \cdot \rho}{r} - \frac{p \cdot \rho^2}{1 + (p-1) \cdot \rho} \right] \cdot f(\alpha, \beta)$$



Assuming the alternative hypothesis ( $\delta$ ) is  $0.4\sigma$  and sample size determination by Elewski D study [13] specified the sample size ( $n$ ) calculated from correlation coefficient ( $\rho$ ), the acceptance interval is 0.06-0.80 (Frison and Pocock, 1992) [15]  $r$  is the number of repeated measurements. In this study,  $r=3$ . The 3 repeated measurements were done on days 7, 14 and 28.  $p$  is the number of qualitative variables. In this study, there was only one qualitative variable, moisturizing product containing MAS064D and desonide cream 0.05% [13]. So,  $p=1$ . Using correlation coefficients 0.60, 0.65, 0.70, 0.75 and 0.80, in formulation, the sample size of each medication is 36.63, 33.77, 30.41, 26.57 and 22.24, respectively. This study selected a correlation

coefficient of ( $\rho$ ) 0.60, so the sample size should be 37 patients per medication. Ten percent drop out is estimated, therefore the final sample size is 41 patients per medication, making the total sample size for 2 medications is 82. However, as each patient received 2 medications, the actual number of patients needed is 41 patients and proceeded to enroll 50 patients.

## Intervention

Pediatric patients, aged 2 weeks to 12 months, with bilaterally symmetrical distribution of mild to moderate ISD, were recruited from 4 centers by 5 pediatric dermatologists, each enrolling 10 subjects from King Chulalongkorn Memorial Hospital, Chulalongkorn University, Ramathibodi Hospital Mahidol University, Queen Sirikit National Institute of Child Health, and Siriraj Hospital Mahidol University. Subjects were excluded from enrolling if they had previous treatment within 2 weeks or had secondary bacterial infection.

Subjects were randomized to treat with either moisturizer containing MAS064D (Sebclair®, Sinclair Pharma plc, Milan, Italy) or 1% hydrocortisone cream on the opposite side of the body (left or right) twice daily, by sequentially numbered bottle from block randomization before the study was started. The moisturizer was repacked in tubes which were identical to 1% hydrocortisone tubes.

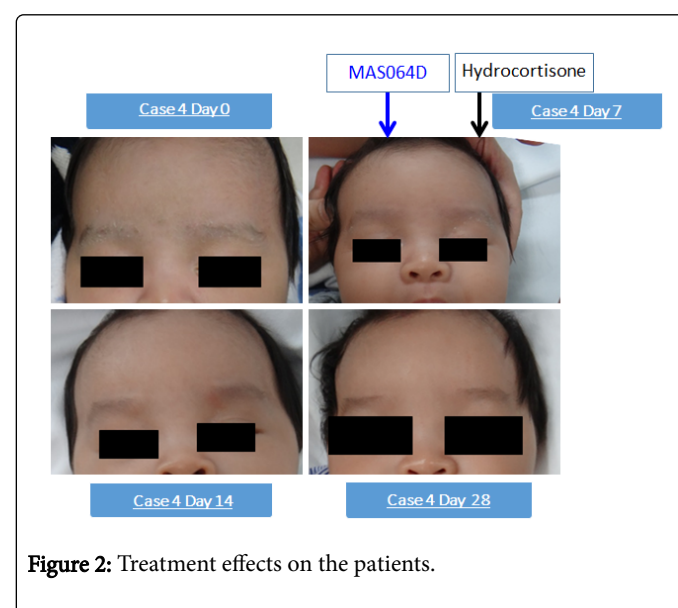
## Assessments

All investigators were able to standardize scoring by using pooled clinical pictures. Total severity score was a composite score (range 0-9) of the clinical presentation of erythema, crust, and scale, each of which were evaluated by a score of 0-3 (0-no lesion, 1-mild, 2-moderate, 3-severe) [10]. Lesions on each side were evaluated on days 0, 6-7, 14 and 28.

## Statistical analysis

Statistical difference was calculated using Wilcoxon signed rank test, with a statistical significance of  $p < 0.05$ .

## Results



Fifty patients (20 females, 30 males) were recruited, 1 patient dropped out because of secondary bacterial infection on day 14. Patient age range was 2 to 48 weeks, with a mean age of 1.8 months. The mean age of onset was 3.2 weeks. Two patients stopped medication on day 14, due to no skin lesion. The most common skin lesion was at the eyebrow (75%), followed by scalp (67%), ear (65%), and trunk (42.9%). Table 1 shows the result of treatment with moisturizer containing MAS064D and 1% hydrocortisone cream. On day 7, moisturizer containing MAS064D had better results than 1% hydrocortisone, but was not statistically significant ( $p=0.052$ ). Both treatments were effective in treatment of ISD in terms of erythema,

crust, scale and total score (Figure 1) from baseline since day 7 ( $p<0.001$ ). There was no significant difference in both treatments (Table 1, Figure 2).

There were 2 patients who reported adverse events on the side decoded as moisturizer containing MAS064D. One patient (2%), reported by his mother, had transient erythema which spontaneously resolved 30 minutes after application. One patient (2%) had a few miliaria. There was no report of adverse events on the side treated with 1% hydrocortisone cream.

	MAS064D		Hydrocortisone		p-value
	n	Mean (95% CI.)	n	Mean (95% CI.)	
Erythema					
Baseline	49	1.67 (1.42, 1.92)	49	1.67 (1.39, 1.95)	1
Day 7	49	0.71 (0.48, 0.94)	49	0.78 (0.54, 1.02)	0.405
Day 14	49	0.47 (0.24, 0.7)	49	0.51 (0.3, 0.72)	0.527
Day 28	47	0.4 (0.2, 0.6)	47	0.32 (0.14, 0.5)	0.248
p-value at day 7		<0.001*		<0.001*	
p-value at day 14		<0.001*		<0.001*	
p-value at day 28		<0.001*		<0.001*	
Crust					
Baseline	49	1.67 (1.44, 1.9)	49	1.65 (1.41, 1.89)	0.655
Day 7	49	0.73 (0.48, 0.98)	49	0.78 (0.54, 1.02)	0.617
Day 14	49	0.39 (0.16, 0.62)	49	0.43 (0.21, 0.65)	0.644
Day 28	47	0.28 (0.11, 0.45)	47	0.36 (0.14, 0.58)	0.463
p-value at day 7		<0.001*		<0.001*	
p-value at day 14		<0.001*		<0.001*	
p-value at day 28		<0.001*		<0.001*	
Scale					
Baseline	49	1.53 (1.27, 1.79)	49	1.53 (1.28, 1.78)	1
Day 7	49	0.69 (0.53, 0.85)	49	0.84 (0.65, 1.03)	0.052
Day 14	49	0.49 (0.29, 0.69)	49	0.59 (0.39, 0.79)	0.132
Day 28	47	0.28 (0.13, 0.43)	47	0.32 (0.18, 0.46)	0.527
p-value at day 7		<0.001*		<0.001*	
p-value at day 14		<0.001*		<0.001*	
p-value at day 28		<0.001*		<0.001*	
Total score					
Baseline	49	4.88 (4.38, 5.38)	49	4.86 (4.31, 5.41)	0.783
Day 7	49	2.14 (1.72, 2.56)	49	2.39 (1.95, 2.83)	0.126
Day 14	49	1.35 (0.88, 1.82)	49	1.53 (1.09, 1.97)	0.254

Day 28	47	0.96 (0.54, 1.38)	47	1 (0.63, 1.37)	0.834
p-value at day 7		<0.001*		<0.001*	
p-value at day 14		<0.001*		<0.001*	
p-value at day 28		<0.001*		<0.001*	
*One case was excluded because of secondary bacterial infection on day 14.					

**Table 1:** The result of treatment with moisturizer containing MAS064D and 1% hydrocortisone cream.

## Discussion

ISD is a self-limited disease in infants. Previous studies have shown that treatment with topical antifungals such as, antifungal shampoo [7] or cream [8,9] and topical anti-inflammatory agents such as topical corticosteroids, licochalcone [10], and MAS064D [14] are all effective.

Active ingredients in the moisturizer containing MAS064D have anti-inflammatory and antifungal activities. Isohexadecane, shea butter, phytosterols and tocopherols, have moisturizing properties. Bisobolol glycyrrhetic acid and alglycer have an anti-inflammatory effect [11,16,17,18]. Piroctone olamine is an antifungal agent that affects *Malassezia spp* [18]. The synergistic effect of antifungal effect, anti-inflammatory and emollients benefit ISD in improving redness, crust, and scale. Clinical studies on the use of moisturizer containing MAS064D in adults and infants have been shown to be effective [11-14,18]. No or mild adverse effects such as slight signs of irritation, rash, itching, and stinging sensation have been reported in some patients. The use of moisturizing products containing MAS064D to treat infantile seborrheic dermatitis has been shown to reduce symptoms by 90% [14]. This study showed that moisturizer containing MAS064D is effective in the treatment of ISD from day 6-7 and had comparable efficacy with 1% hydrocortisone. Both treatments were effective in treatment of ISD in terms of erythema, crust, and scale from baseline since day 7.

Adverse events of moisturizer containing MAS064D is transient and occurred in 2 patients who reported on the side that was decoded as moisturizer containing MAS064D. One patient had transient erythema which spontaneously resolved in 30 minutes on the first day after application. One patient (2%) had a few miliaria on the moisturizer containing MAS064D side which contains isohexadecane and shea butter as an emollient. This cream is thicker than 1% hydrocortisone cream made from King Chulalongkorn Memorial Hospital and could have made it easier to cause miliaria.

## Conclusion

Moisturizer containing MAS064D cream is effective and safe in the treatment of ISD. Since ISD is a chronic and relapsing disease, MAS064D cream can be used in patients with ISD whom do not want to use topical corticosteroids.

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