Therapeutic Efficacy and Safety of Loratadine Syrup in Childhood Atopic Dermatitis Treated with Mometasone Furoate 0.1 Per Cent Cream

AMORNSRI CHUNHARAS, M.D.*, WANEE WISUTHSAREWONG, M.D.**,
SIRIWAN WANANUKUL, M.D.***, SUCHITRA VIRAVAN, M.D.**

Abstract

Atopic dermatitis is a common skin disease in Thai children. The treatment of atopic dermatitis requires topical corticosteroids, emollients, systemic antihistamine as well as avoidance of the precipitating factors. A double blind multicenter placebo controlled study was conducted to assess the therapeutic efficacy of topical mometasone furoate 0.1 per cent cream in combination with loratadine syrup. Forty-eight patients, 23 boys and 25 girls, mean age 73.67 months, with atopic dermatitis were included in the study. The severity of the disease was measured by using the SCORAD index including the degree of erythema, dryness, edema/papulation, oozing/crusting, lichenification, and excoriation. Total area involved was measured and a target area of dermatitis was selected for specific evaluation. The degree of clinical signs and pruritic symptom was graded. The sensation of pruritus, disturbance of sleep due to pruritus, and feeling of sleepiness in the morning were recorded. Mometasone furoate 0.1 per cent cream was applied to all patients once daily. One group received loratadine syrup and another group received placebo syrup. They were followed-up on day 5, 8 and 15. The severity of atopic dermatitis and pruritus significantly decreased after 14 days of treatment in both groups ($p < 0.001$). There was no difference in therapeutic response between the loratadine and placebo groups ($p = 0.99$). All signs examined had decreased by the end of the study. The result demonstrated that 0.1 per cent mometasone therapy is very effective for treating childhood atopic dermatitis. Loratadine did not show beneficial effect when combined with good topical corticosteroid but it was safe and had no serious side effect on the children.

Key word : Atopic Dermatitis, Mometasone Furoate, Loratadine

**CHUNHARAS A, WISUTHSAREWONG W,
WANANUKUL S, VIRAVAN S
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* Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400,
** Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700,
*** Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

Atopic dermatitis is a chronic relapsing pruritic inflammatory skin disease. It is common in pediatric practice with a prevalence around 13.4 per cent in Thai schoolchildren[1]. The treatment of atopic dermatitis requires topical corticosteroids, emollients, systemic antihistamine as well as avoidance of the precipitating factors such as some types of food and airborne allergens. Topical corticosteroid is the mainstay of therapy to control the acute flare up of the disease. The least potent corticosteroid that controls the patient's symptoms should be used. Many kinds of topical corticosteroids have been introduced. Mometasone furoate 0.1 per cent cream is a moderate potency topical corticosteroid which has been previously described as having excellent anti-inflammatory and anti-pruritic activities with less inhibitory effect on the hypothalamic-pituitary-adrenal axis (HPA)[2-6]. Since pruritus is often a symptom of atopic dermatitis, antihistamines with sedative effect are commonly prescribed. Many sedative antihistamines have a direct effect on pruritus and help the child to fall asleep, but morning drowsiness limits their use in schoolchildren. Loratadine, non-sedating H_1 antihistamine, has shown beneficial effects on pruritus, severity of rash in patients with allergic skin diseases and atopic dermatitis when compared to placebo, and hydroxyzine[7-9]. The combination of topical mometasone furoate 0.1 per cent cream and oral loratadine is expected to reduce signs and symptoms of patients with atopic dermatitis.

MATERIAL AND METHOD

This was a double blind multicenter comparative study designed to study the efficacy, safety and side effect of once-daily oral loratadine in controlling itching, and improvement of signs and symptoms in childhood atopic dermatitis. The protocol of the study was approved by the Ethics Review Committee on Research Involving Human Subjects of the Faculty of Medicine, Siriraj Hospital, Mahidol University.

Patients

Atopic dermatitis patients were studied at Chulalongkorn Hospital, Ramathibodi Hospital and Siriraj Hospital from May 1998 to December 1998. They were diagnosed by using criteria of the UK. Atopic Dermatitis Diagnostic Criteria Working Party by Williams et al (Table 1)[10-12]. Inclusion criteria included: patients of either sex, aged 2-12 years and in need of treatment for eczema. Evaluation was done before starting the medication and at each visit. The severity of the disease was measured by using the SCORAD index including the degree of erythema, dryness, edema/papulation, oozing/crusting, lichenification, and excoriation. The degree of clinical signs and pruritus symptom was graded from 0 (none) to 3 (severe) scale (Table 2). Total area involved was measured and a target area of dermatitis was selected for specific evaluation. The size of the target lesion should not be less than 4 square centimeters and the sum of the severity scores must be at least 10 out of 18. Pruritus at the target area must be present at baseline with a severity of at least 2.5. The patients should be healthy without history or physical signs of other skin infections, skin diseases or other illnesses. A signed informed consent was obtained from a parent of each child before enrollment. The exclusion criteria included patients who had a history of hypersensitivity to these drugs or were nonresponsive to mometasone before the study. The patients should not receive topical corticosteroids, oral corticosteroid, corticosteroid injection, PUVA therapy, any kind of antibiotics or antifungals, short acting antihistamines, long acting antihistamines, ketotifen or azelastine, astemizole within 14 days, 30 days, 90 days, 14 days, 7 days, 12 hours,

Table 1. The diagnostic criteria for atopic dermatitis by the UK Working Party[10].

Itchy skin condition plus three or more of the followings:
1. History of flexural involvement (or cheeks in infants)
2. History of asthma/hay fever (or first-degree relative in children less than 4 years old)
3. History of generalized dry skin
4. Visible flexural dermatitis (or cheeks in infants)
5. Onset of rash under 2 years old

Table 2. SCORAD index.

Signs	SCORAD index			
	None/Complete absence (0)	Mild/slight (1)	Moderate/ definitely present (2)	Severe/quite marked, Intense (3)
Erythema	0	1	2	3
Dryness	0	1	2	3
Edema/papulation	0	1	2	3
Oozing/crusting	0	1	2	3
Lichenification	0	1	2	3
Excoriation	0	1	2	3

Table 3. Data of the study group.

	Loratadine	Placebo	P-value
Total cases	24	24	1.000
Male:Female	11:13	12:12	1.000
Mean age (month)	71.04 ± 36.82	76.29 ± 32.65	0.604
Starting weight (kg)	23.00 ± 8.42	23.82 ± 8.11	0.735
Ending weight (kg)	23.01 ± 8.36	24.08 ± 8.23	0.665
Personal history of allergy (%)	83.33	58.33	0.112
Family history of allergy (%)	83.33	70.83	0.492
Mean target area (sq cm)	35.30 ± 32.84	32.29 ± 29.40	0.742
Mean total area (% BSA)	22.56 ± 15.03	18.17 ± 16.18	0.335

4 days, 2 weeks, 3 months before enrollment. All side effects, illness, and other medications used during the study were monitored. If antibiotics or antihistamine were used or severe illness and side effects were noted, the patient was withdrawn from the study.

The patients were told to apply 0.1 per cent mometasone furoate (Elomet, Schering-Plough Corp.) once daily after a bath in the evening as well as taking once daily 5 ml of an unknown syrup/30 kg in the evening. Patients who weighed more than 30 kilograms should take two teaspoonfuls. They should record timing of medication in the report card and show it to the investigator at every visit. They were followed-up at day 5, 8 and 15. At the end of the study, codes of the unknown syrups were opened in order to ascertain the results of the study.

Clinical evaluation

The signs and symptoms of the patients were recorded at the target site at every visit. The SCORAD index scale was measured to indicate the intensity of the total involved areas. Physical global evaluation was graded as cleared (100% improvement of sign and symptom except for residual discoloration), marked improvement (75-100% clearance of sign and symptom compared to baseline), mode-rate improvement (50-75% improvement of sign and symptom compared to baseline), slight improvement (<50% improvement of sign and symptom compared to baseline), no change (no detectable improvement of sign and symptom compared to baseline) and exacerbation (flare up of the treatment areas). Rating of pruritic symptom was 0 (none) to 3 (severe). Efficacy of loratadine was assessed from the report form in relation to the sensation of pruritus, disturbance of sleep due to pruritus, and feeling of sleepiness in the morning. The data were analyzed by student's *t*-tests.

RESULT

Fifty patients met the criteria and were enrolled in the study. Two patients in the loratadine group were excluded from the study because one developed impetigo after seven days of treatment; otherwise the skin lesion improved in nearly 90 per cent

Table 4. Results of the study.

	Loratadine	Placebo	P-value
SCORAD index			
D 1	12.40 ± 2.78	12.21 ± 2.11	0.794
D 5	5.88 ± 3.11	4.90 ± 2.61	0.243
D 8	3.10 ± 2.38	2.79 ± 2.21	0.639
D 14	1.94 ± 2.25	1.83 ± 2.61	0.883
Pruritus			
D 1	2.77 ± 0.36	2.63 ± 0.47	0.235
D 5	1.10 ± 0.66	0.85 ± 0.60	0.176
D 8	0.52 ± 0.70	0.29 ± 0.41	0.175
D 14	0.29 ± 0.53	0.09 ± 0.25	0.097

Table 5. Physical global evaluation.

	Loratadine %	Placebo %	P-value
D 5			
< 50% improvement	33.33	25.00	0.751
50-75% improvement	45.83	33.33	0.555
75-100% improvement	20.83	41.67	0.213
D 8			
< 50% improvement	8.33	4.17	1.000
50-75% improvement	29.17	16.67	0.492
75-100% improvement	62.50	79.17	0.341
D15			
< 50% improvement	16.67	0.00	0.109
50-75% improvement	8.33	8.33	1.000
75-100% improvement	75.00	91.67	0.245

at the first visit (fifth day). Another patient was withdrawn from the follow-up on day 8 because the rash was very much improved. At the end of the study 48 patients were analyzed. There were twenty-four patients in each group with 23 boys and 25 girls. The ages ranged from 24.0 to 133.0 months with the mean age of 73.67 ± 34.53 months. There was no difference in sex ratio, age, starting weight, SCORAD index of total involved areas, severity at the target site, mean study area, total area involvement, pruritus score at the beginning of the study (Table 3, 4). At the end of the study 83.3 per cent in the loratadine group and 100.0 per cent in the placebo group showed marked improvement with cleareance of both skin lesion and pruritus (Table 5). The severity of atopic dermatitis and pruritus decreased significantly after 14 days of treatment in both groups ($p < 0.001$) but there was no difference in therapeutic response between the loratadine and placebo groups ($p = 0.99$). All signs examined including erythema, dryness, papulation, oozing, lichenification, and excoriation statistically decreased by the end of the study. The SCORAD index showed improvement from the second visit. On the fifth day of treatment, SCORAD index decreased from 12.40 to 5.88 in the loratadine group and from 12.21 to 4.90 in the placebo group. No patient in both groups reported drowsiness or difficulty in awakening. There were two patients who reported dizziness, one in the loratadine group and one in the placebo group. One in the loratadine group had nausea and one in the placebo group had anorexia. The weight of the patients in the loratadine group at the end of the study showed no change from the beginning (p 0.25).

DISCUSSION

The result of this study is similar to previous studies showing that 0.1 per cent mometasone

furoate therapy is very effective for treating childhood atopic dermatitis[2,13]. The clinical signs of the patients improved very fast after treatment. The pruritic symptom decreased when the severity of the disease decreased. From this study, loratadine did not show beneficial effect when combined with good topical corticosteroid such as mometasone furoate cream. However, loratadine was demonstrated to be safe and had very few side effects on the children. There was no complaint of sleepiness or drowsiness in the patients treated with loratadine. If antihistamine is needed in atopic dermatitis patients who have pruritus or other allergic reactions, loratadine is one of the drugs of choice in order to avoid sedative side effects especially children who have to go to school.

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การศึกษาประสิทธิภาพและความปลอดภัยของการรับประทานยาลอราตาดีนร่วมกับการทาครีม 0.1% โมเมทาโซน ฟูโรเอท ในการรักษาผู้ป่วยเด็กที่เป็นโรคผิวหนังภูมิแพ้

อมรศรี ชุณหรัศมิ์, พ.บ., วาณี วิสุทธิ์เสรีวงศ์, พ.บ.**, ศิริวรรณ วนานุกูล, พ.บ.***, สุจิตรา วีรวรรณ, พ.บ.***

โรคผิวหนังภูมิแพ้เป็นโรคที่พบบ่อยมากโรคหนึ่งในเด็ก อาการคันเป็นปัญหาใหญ่ซึ่งทำให้เด็กนอนไม่หลับและอาจเกาจนผิวหนังอักเสบเป็นแผล หลักการรักษาทั่วไปคือการหลีกเลี่ยงสิ่งระคายเคืองต่าง ๆ การทายาคอร์ติโคสตีรอยด์ซึ่งมีหลายตัวที่สามารถใช้ได้ผลดี การรับประทานยาแอนตี้ฮิสตามีนจะช่วยลดอาการคันเพื่อไม่ให้เด็กเกา แต่เนื่องจากแอนตี้ฮิสตามีนที่ใช้ทั่ว ๆ ไป มีฤทธิ์ทำให้เกิดอาการง่วงนอนจึงอาจมีปัญหาผลต่อการเรียนหนังสือ ปัจจุบันมีการพัฒนายาแอนตี้ฮิสตามีนตัวใหม่ ๆ ขึ้นมาช่วยในการรักษาและลดปัญหาง่วงนอน ยาลอราตาดีนเป็นแอนตี้ฮิสตามีนตัวหนึ่งที่มีคุณสมบัติช่วยลดอาการคันและไม่ทำให้ง่วงนอน การศึกษานี้ทำเพื่อศึกษาประสิทธิภาพและความปลอดภัยของการทาครีม 0.1% โมเมทาโซน ฟูโรเอท ร่วมกับการรับประทานยาลอราตาดีนเปรียบเทียบกับการรับประทานยาหลอก การศึกษาทำโดยหลายสถาบันร่วมกันและผู้ป่วยรวมทั้งแพทย์ผู้ประเมินผลไม่ทราบชนิดของยาที่ผู้ป่วยได้รับ ผู้ป่วยเด็กที่ศึกษาเป็นโรคผิวหนังภูมิแพ้จำนวน 48 ราย อายุเฉลี่ย 73.67 เดือน ทุกคนทายาโมเมทาโซน ฟูโรเอท ผู้ป่วยกลุ่มหนึ่งรับประทานยาลอราตาดีนและอีกกลุ่มรับประทานยาหลอก ผลการรักษาดูจากระดับความรุนแรงของความแดง ความแห้งของผิวหนัง ตุ่มนูน ตุ่มน้ำ ความหนาของรอยโรค รอยเกาและอาการคัน ผลการศึกษาพบว่าผู้ป่วยทุกรายมีความรุนแรงของโรคและอาการคันลดลงอย่างชัดเจนภายหลังการรักษา 14 วัน โดยอาการเริ่มดีขึ้นตั้งแต่วันที่ 5 ไม่พบความแตกต่างระหว่างกลุ่มที่รับประทานยาลอราตาดีนเมื่อเปรียบเทียบกับยาหลอก และไม่พบผลข้างเคียงของยาลอราตาดีน จึงน่าจะสรุปได้ว่ายาโมเมทาโซน ฟูโรเอท เป็นยาทาที่ได้ผลดีมากในการรักษาผู้ป่วยโรคผิวหนังภูมิแพ้ไม่ว่าจะใช้ยาแอนตี้ฮิสตามีนร่วมด้วยหรือไม่ ส่วนลอราตาดีนเป็นยาแอนตี้ฮิสตามีนที่ปลอดภัยในเด็ก ไม่มีผลข้างเคียงที่ทำให้เด็กง่วงนอน สามารถใช้ร่วมกับยาทาคอร์ติโคสตีรอยด์ได้ในกรณีที่มีข้อบ่งชี้ในการใช้ยาแอนตี้ฮิสตามีนในการรักษาผู้ป่วยเด็กที่มีภาวะผิวหนังอักเสบร่วมกับภาวะภูมิแพ้อื่น ๆ

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อมรศรี ชุณหรัศมิ์, วาณี วิสุทธิ์เสรีวงศ์, ศิริวรรณ วนานุกูล, สุจิตรา วีรวรรณ
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* ภาควิชากุมารเวชศาสตร์, คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10400
** ภาควิชากุมารเวชศาสตร์, คณะแพทยศาสตร์ศิริราชพยาบาล, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10700
*** ภาควิชากุมารเวชศาสตร์, คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย, กรุงเทพ ฯ 10330