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Original Article

Efficacy comparison of cetirizine and loratadine for allergic rhinitis in children

Juliana, Rita Evalina, Lily Irsa, M. Sjabaroeddin Loebis

Abstract

Background Allergic rhinitis represents a global health problem affecting 10% to more than 40% of the population worldwide. Several studies in recent years have described the efficacy of second-generation antihistamines in younger children. It is not well established whether cetirizine is more effective than loratadine in reducing symptoms of allergic rhinitis.

Objective The objective of this study was to compare the efficacy of loratadine with cetirizine for treatment of allergic rhinitis.

Methods We conducted a randomized, double-blind, controlled trial of 100 children, aged 13 to 16 years, from October to November 2009 at two junior high schools in Medan. Group I received 10 mg of cetirizine and group II received 10 mg of loratadine, each once daily in the morning for 14 days. Drug efficacy was assessed by changes from baseline symptom scores and evaluation of therapeutic responses after 3 days, 7 days and 14 days of treatment.

Results The efficacy of cetirizine compared to that of loratadine was not statistically significant in diminishing nasal symptoms after 3 days, 7 days and 14 days of treatment (P=0.40, P=0.07, and P=0.057, respectively). Evaluation of side effects, however, revealed significantly fewer headaches in the cetirizine group after 3 days and 7 days of treatment (P=0.01 and P=0.03, respectively) than in the loratidine group. In addition, the loratadine group had significantly more instances of palpitations after 7 days of treatment (P=0.04) compared to the cetirizine group.

Conclusion There was no significant difference in cetirizine and loratadine treatment effectiveness on allergic rhinitis. However, loratadine was found to cause more headaches and palpitations than cetirizine. **[Paediatr Indones. 2012;52:61-6]**.

Keywords: *antihistamines, cetirizine, loratadine, allergic rhinitis*

Allergic rhinitis (AR) is a global health problem, affecting 10% to more than 40% of the population worldwide.[1,2] Symptomatic allergic rhinitis reduces quality of life and may contribute to impairment of psychological well-being and cognitive function.[3]

Antihistamines are the pharmacologic cornerstone of treatment for allergic rhinitis.[4] The comparative effects of second generation antihistamines, cetirizine and loratadine, among younger patients have not been well documented. Cetirizine and loratadine are antagonists to the histamine H1 receptor and their metabolism may lead to sedative and cardiotoxic effects. Thus, more research on these drugs is needed.[5,6]

Loratadine is 98% metabolized in the liver and excreted by the kidneys, while cetirizine metabolism does not involve the liver, though it is mostly excreted by the kidneys. However, Bucks et al found that cetirizine is six times more potent than loratadine, thus a higher dose of loratadine is often required to

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From the Department of Child Health, University of North Sumatra Medical School, Adam Malik Hospital, Medan.

Reprint requests to: Juliana, MD, Department of Child Health, Medical School, University of North Sumatera/Adam Malik Hospital, Jl. Bunga Lau No.17, Medan. Ph. +62-61-8361721/8365663, Fax. +62-61-8361721. Email: *Juliana.md@live.com*

achieve a similar result.[6] Other second generation antihistamines, such as terfenadine and astemizole, also had similar effects compared to cetirizine, but these drugs are metabolized rapidly in the liver and have cardiotoxic effects.[6,7] The purpose of this study was to compare the efficacy of cetirizine and loratadine for treatment of allergic rhinitis in children.

Methods

We conducted a randomized, double-blind, controlled trial from October to November 2009 at two junior high schools in Medan. Data were collected by questionnaire. Patients were enrolled in the study if they had symptoms of allergic rhinitis (runny nose, sneezing, nasal stuffiness, eye itchiness, eye redness, sleep disturbance, impaired cognitive functioning, or school absence) and were atopic. We included children aged 13 to 16 years, who were diagnosed with allergic rhinitis that was confirmed by nasal examination. To evaluate severity of the disease, we used a rhinitis allergic scoring system: 0= no evident symptoms, 1= mild symptoms not interfering with daily activities and/or sleep, 2= moderate symptoms somewhat interfering with daily activities and/or sleep, and 3= severe symptoms with major

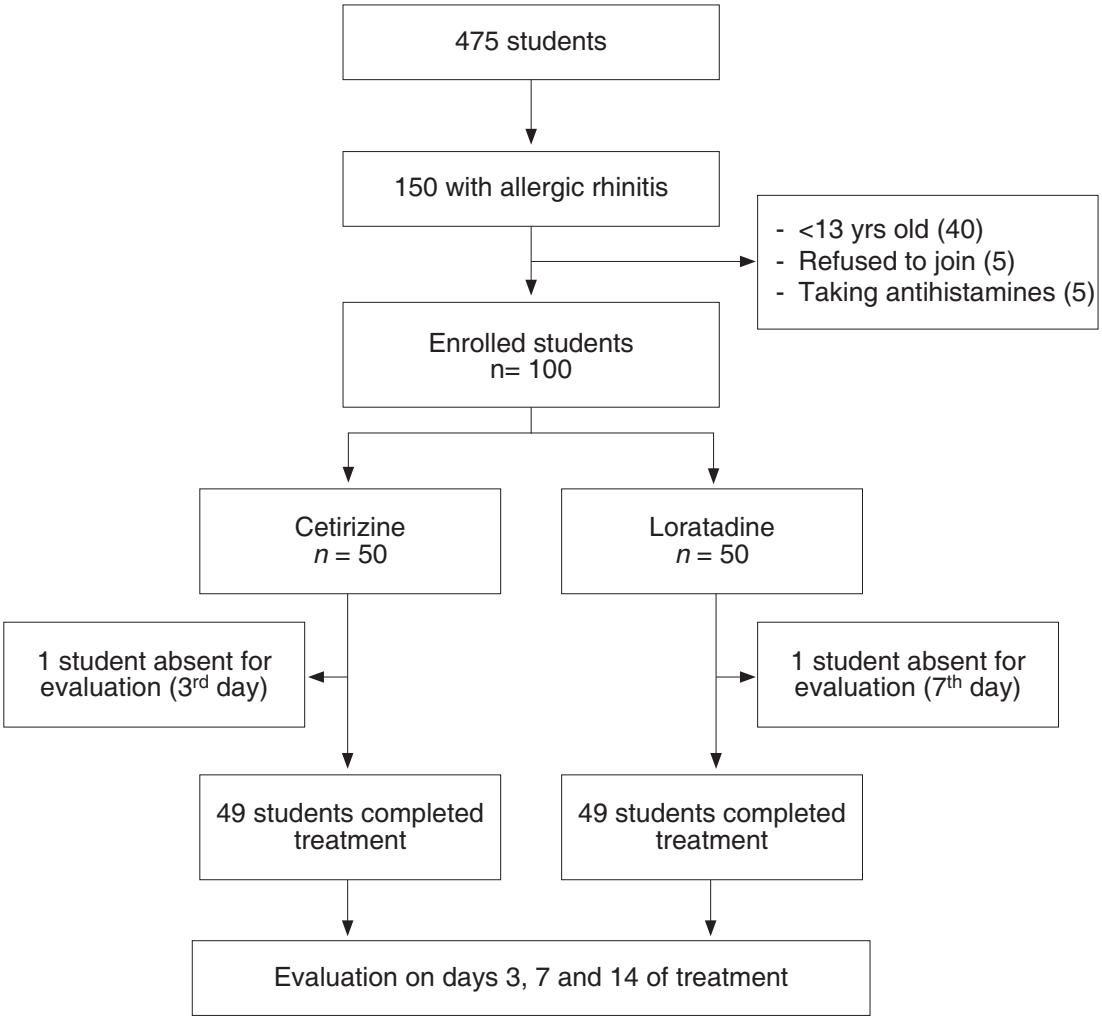

Figure 1. Study profile

interference in daily activities and/or sleep.[11] We excluded subjects with a history of documented asthma, sinusitis, common cold, otitis media, nasal anatomic abnormalites, known idiosyncratic reactions to cetirizine or loratadine, corticosteroid use within two weeks of the first test dose, oral or topical decongestant and antihistamine use within 24 hours of the first test dose, and those who refused to consume the drug.

Patients were divided into two groups by simple randomization using random tables. Group I received 10 mg cetirizine and group II received 10 mg loratadine, with each medication taken once a day orally for 14 days. We evaluated the patients at visit 1 for screening, after 3 days (visit 2), after 7 days (visit 3) and after 14 days (visit 4) of treatment. Subjects were not allowed to consume other antihistamines or corticosteroids during treatment period.

Treatment efficacy was assessed by changes from baseline symptom scores and side effects were assessed after therapeutic response at 3 days, 7 days, and 14 days of treatment. Symptoms were observed and physical examination was performed at each visit. This study was approved by the Ethics Committee of the Medical School University of North Sumatera.

Chi-square test was performed to analyze treatment efficacy and side effects. Differences were considered significant if $P< 0.05$. We used SPSS version 15 for data processing. Our study was an intention to treat analysis.

Results

We screened 475 students, of which 150 suffered from allergic rhinitis. Fifty of these students were excluded for the following reasons: 40 students were aged below 13 years, 5 students refused to participate, and 5 students were already taking antihistamines. The remaining 100 students were randomized into two groups of 50, each of whom received treatment with 10 mg loratadine or 10 mg cetirizine (**Figure 1**).

Subjects' characteristics are shown in **Table 1**. The mean age in the cetirizine group was 13.40 years while in that of the loratadine group was 13.38 years. There were 34 females in the cetirizine group (68%) and 29 in the loratadine group (58%). At the first visit, 21 students in the cetirizine group had a moderate allergic rhinitis score while 29 students had a severe score. In the loratadine group, 16 had moderate and 34 had severe scores. The majority of subjects (63%) had severe allergic rhinitis scores at baseline.

Table 2 shows scores of allergic rhinitis at days 3, 7, and 14 of treatment. On days 3 and 7, there were decreased symptoms of rhinitis in both groups, but there was no statistically significant difference between the two groups ($P=0.40$ for day

Table 1. Baseline characteristics

Characteristics	Cetirizine, n (%)	Loratadine, n (%)
Sex		
Male	16 (32)	21 (42)
Female	34 (68)	29 (58)
Age		
13 years old	30 (60)	32 (64)
14 years old	15 (30)	10 (20)
15 years old	5 (10)	8 (16)
Mean age, years	13.40	13.38
Symptoms		
Runny nose	45 (90)	42 (84)
Sneezing	49 (98)	49 (98)
Stuffiness	44 (88)	48 (96)
Eye itchiness	17 (34)	18 (36)
Eye redness	18 (36)	16 (32)
Sleep disturbance	31 (62)	31 (62)
Impaired school performance	27 (54)	39 (78)
School absence	5 (10)	10 (20)
Allergic rhinitis score		
Moderate	21 (42)	16 (32)
Severe	29 (58)	34 (68)

Table 2. Scores of allergic rhinitis at days 3, 7, and 14 of treatment.

Evaluated scores rhinitis	Cetirizine n(%)	Loratadine n(%)	P
Day-3			0.400
Mild	3 (6)	1 (2)	
Moderate	30 (60)	27 (54)	
Severe	17 (34)	22 (44)	
Day-7			0.070
No symptoms	18 (36)	10 (20)	
Mild	4 (8)	9 (18)	
Moderate	26 (52)	24 (48)	
Severe	2 (4)	7 (14)	
Day-14			0.057
No symptoms	43 (86)	37 (74)	
Mild	6 (12)	5 (10)	
Moderate	0 (0)	7 (14)	
Severe	1 (2)	1 (2)	

Table 3. Clinical symptoms evaluation on days 3, 7 and 14 after cetirizine or loratadine treatment

Symptoms	Day 3		P	Day 7		P	Day 14		P
	cetirizine n (%)	loratadine n (%)		cetirizine n (%)	loratadine n (%)		cetirizine n (%)	loratadine n (%)	
Runny nose	40 (80)	36 (72)	0.34	24 (48)	27 (54)	0.15	2 (4)	2 4)	1.00
Sneezing	40 (80)	44 (88)	0.20	27 (54)	34 (68)	0.15	2 (4)	7(14)	0.08
Stiffness	33 (66)	34 (68)	0.83	19 (38)	27 (54)	0.10	3 (6)	6(12)	0.29
Eye itchiness	9 (18)	13 (26)	0.33	4 (8)	9 (18)	0.13	2 (4)	4 (8)	0.40
Eye redness	7 (14)	6 (12)	0.76	5 (10)	6 (12)	0.74	1 (2)	2 (4)	0.92
Sleep disturbance	6 (12)	11 (22)	0.18	2 (4)	5 (10)	0.24	0 (0)	2 (4)	0.15
Impaired school performance	6 (12)	11 (22)	0.18	4 (8)	9 (18)	0.13	0 (0)	3 (6)	0.07
School absence	1 (2)	2 (4)	0.55	1 (2)	1 (2)	1.00	1(2)	1 (2)	1.00

Table 4. Side effects on day 3, 7 and 14 of cetirizine or loratadine treatment

Side effects	Day 3		P	Day 7		P	Day 14		P
	cetirizine n (%)	loratadine n (%)		cetirizine n (%)	loratadine n (%)		cetirizine n (%)	loratadine n (%)	
Sedation	22 (44)	19 (38)	0.48	24 (48)	17 (34)	0.15	22 (44)	18 (36)	0.41
Dizziness	12 (24)	12 (24)	0.62	16 (32)	10 (20)	0.17	9 (18)	9 (18)	1.00
Confusion	5 (10)	6 (12)	0.74	7 (14)	4 (8)	0.33	4 (8)	7 (14)	0.33
Bitter taste	19 (38)	21 (42)	0.68	15 (30)	21 (42)	0.21	13 (26)	17 (34)	0.38
Nausea	11 (22)	10 (20)	0.86	11 (22)	8 (16)	0.44	5 (10)	4 (8)	0.72
Vomiting	2 (4)	2 (4)	1.00	5 (10)	1 (2)	0.09	1 (2)	1 (2)	1.00
Dry mouth	23 (46)	25 (50)	0.68	21 (42)	17 (34)	0.41	16 (32)	12 (24)	0.37
Headaches	4 (8)	13 (26)	0.01	8 (16)	17 (34)	0.03	6 (12)	10 (20)	0.27
Breathing difficulty	2 (4)	6 (12)	0.14	4 (8)	5 (10)	0.72	2 (4)	3 (6)	0.64
Urinary incontinence	1 (2)	4 (8)	0.16	2 (4)	5 (10)	0.24	1 (2)	0 (0)	0.31
Tiredness	13 (26)	18 (36)	0.27	14 (28)	18 (36)	0.39	12 (24)	11 (22)	0.81
Palpitations	5 (10)	2 (4)	0.23	0 (0)	4 (8)	0.04	0 (0)	2 (4)	0.15
Blurred vision	1 (2)	2 (4)	0.55	4 (8)	2 (4)	0.40	3 (6)	1 (2)	0.30

3 and P=0.07 for day 7). On day 14, the majority of subjects in both groups were free from symptoms, but difference in the two groups was also not statistically significant (P=0.057).

Table 3 reports the observation of symptoms after 3, 7, and 14 days of treatment. There was improvement in symptoms in each group, but there were no statistically significant differences between the two groups.

Table 4 shows the incidence of side effects after 3, 7, and 14 days of treatment. There were significant differences between the two groups after 3 days and 7 days of treatment. Headaches were more frequently present in the loratadine group compared to the cetirizine group (day 3, P=0.01 and day 7, P=0.03). In addition, at 7 days, we observed more palpitations in the loratadine group than in the cetirizine group (P=0.04).

Discussion

An estimated 20 to 40 million Americans are affected by allergic rhinitis. The actual prevalence of the condition is difficult to discern as many sufferers self-medicate without seeking medical care.[8] According to the International Study on Asthma and Allergy in Childhood (ISAAC), the prevalence of allergic rhinitis is 1.4 - 39.7% at the age of 13 to 14 years.[1,2] In agreement, we found 32% (150/475) of students screened to have this condition. Our subjects' mean age was 13.4 years.

The diagnosis of allergic rhinitis is usually made on the basis of the patient's history and the results of physical examination. In addition to classic symptoms of nasal congestion, itchy nose, sneezing, rhinorrhea, and itchy, watery eyes, other important considerations include a family history of allergic rhinitis, a history of

other atopic diseases, previous treatment experiences and suspected triggers.[8] For the purposes of our study, the diagnosis of allergic rhinitis was made from assessing classic symptoms, obtaining a family history of allergic rhinitis, a history of other atopic diseases and physical examination.

We did not perform diagnostic tests to establish the allergic rhinitis diagnosis because many subjects refused to give blood samples nor consent to patient skin prick tests. Published guidelines from the American Academy of Asthma, Allergy and Immunology, as well as other expert panels, recommended confirmatory testing when allergic rhinitis is clinically suspected. There is no evidence to support the superiority of this recommendation over direct empiric trial of medications, and most primary care physicians choose to treat empirically based upon the history and physical examination.

Diagnostic tests include skin prick testing, intradermal testing, and in vitro blood tests. Nasal challenge testing, nasal smears, sinus transillumination, and nasopharyngoscopy are non-specific tests. Non-specific tests are not recommended for routine evaluation, but may be useful in selected cases when allergen specific tests have failed to clarify the causes of rhinitis.[8]

Second-generation antihistamines are selective for peripheral H1 receptors. These agents are associated with less sedative anticholinergic effects than non-selective first-generation antihistamines.[6] The efficacy and safety of some second-generation antihistamines in children have been assessed in a number of well-designed clinical trials.[9,10] In contrast with our findings, a study in Mexico reported that 10 mg of cetirizine can reduce the major symptoms of allergic rhinitis (runny nose, sneezing, itchy nose, and watery eyes) better than loratadine and placebo.[4] Our study showed no significant difference in the effectiveness of loratadine and cetirizine in treating allergic rhinitis.

The majority of our participants suffered from severe allergic rhinitis based on the scoring system we used. We classified the allergic rhinitis symptoms into categories of mild, moderate and severe. Mild was defined as no interference with daily activities and/or sleep. Moderate was defined as some interference with daily activities and/or sleep. And severe was defined as significant/major interference with daily activities and/or sleep.[11]

We found no significant difference in sedative effect between the cetirizine group and the loratadine group after 3, 7, and 14 days of treatment ($P=0.48$, $P=0.15$, $P=0.41$, respectively). In contrast, studies in Mexico and the USA reported a significantly higher sedative side effects in the cetirizine group than in the loratadine group ($P<0.001$).[4,12] Another review showed the side effects (such as headaches) of both cetirizine and loratadine were about 1 to 12%.[9] But a clinical study on loratadine reported no sedative or anticholinergic effect, which was clinically significant when this drug was compared to placebo.[13]

A study of 398 patients was conducted to determine the effects of cetirizine on health-related quality of life in patients with seasonal allergic rhinitis. Cetirizine was shown to be efficacious for total symptom severity, as well as for quality of life measures including activities of daily living, practical problems, symptom distress, sleep disturbance, and emotional difficulties.[14] Similar to our study, the symptoms of sleep disturbance and impaired school performance decreased following the end of treatment with cetirizine, but no statistical difference was shown compared to loratadine group.

Second-generation antihisitmines such as cetirizine, loratadine, fexofenadine and ebastine are thought to have cardiotoxic effects such as hypertension, hypotension, palpitation, supraventricular tachyarrhythmia, syncope and tachycardia, though plasma concentrations are higher compared to astemizol and terfenadin.[15] Our study found statistically significant differences in the presence of palpitations between the two groups on day 7 of treatment.

We conclude there was no significant difference between cetirizine and loratadine in treatment effectiveness of allergic rhinitis. However, loratadine was more frequently associated with side effects of headaches and palpitations.

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