

Comparison of the Efficacy of Olopatadine and Fexofenadine in Chronic Idiopathic Urticaria Patients: A Crossover Study

Hideaki Tanizaki^a Yosuke Yamamoto^{a,c} Satoshi Nakamizo^a Atsushi Otsuka^a
Yoshiki Miyachi^a Kenji Kabashima^a

^aDepartment of Dermatology, ^bInstitute for Advancement of Clinical and Translational Science, Kyoto University Hospital Department of Clinical Epidemiology, and ^cDepartment of Healthcare Epidemiology, Kyoto University Graduate School of Medicine, Kyoto, Japan

Key Words

Olopatadine · Antihistamine · Urticaria

Abstract

Olopatadine is one of the second-generation H₁ antihistamines that were used for treating allergic disorders initially in Asia, and now also in Western countries. Whereas several trials compared the efficacy on chronic urticaria among second-generation H₁ antihistamines, no study has directly compared the clinical efficacy between olopatadine and other H₁ antihistamines in patients with chronic idiopathic urticaria (CIU). In this study, we address this issue for the first time and conclude that olopatadine is a good candidate for the treatment of CIU.

© 2015 S. Karger AG, Basel

Introduction

Urticaria is a common dermatologic disease that affects up to 20% of the general population. Three quarters of cases of chronic urticaria fall into the category of chronic idiopathic urticaria (CIU). CIU is generally mediated by histamines [1] and requires treatment in order to regulate symptoms that impair work productivity. Second-generation histamine receptor H₁ antagonists have been developed

which significantly reduce the incidence of centrally mediated and anticholinergic side effects [2]. Although there is the notion that commonly employed H₁ antihistamines are equally efficacious and safe when used in the management of allergic diseases, a review of the pharmacological properties has indicated differences among these agents with respect to their pharmacokinetic and pharmacodynamic properties. These dissimilar characteristics may lead to differences in overall potency and potential toxicity [3].

Olopatadine is one of the second-generation non-sedating H₁ antihistamines that were used initially in Asia, and now also in Western countries, to treat allergic disorders, such as urticaria, rhinitis, and atopic dermatitis [4]. Olopatadine is known to exhibit inhibitory effects on the release of inflammatory lipid mediators, such as leukotriene and thromboxane from human polymorphonuclear leukocytes and eosinophils [5]. Whereas several trials compared the efficacy of second-generation H₁ antihistamines on CIU [6–8], no study has directly compared the clinical efficacy of olopatadine to that of other H₁ antihistamines in patients with CIU.

Methods

To this end, 40 patients with CIU were enrolled in this study. All patients were examined thoroughly using general and systemic examinations to rule out any septic focus or any obvious causes

Table 1. Baseline characteristics of each group

Characteristic	Group 1 (olopatadine first, n = 20)	Group 2 (fexofenadine first, n = 20)	p value
Age, years	50.5 (8.7)	51.0 (9.5)	0.88
Male, %	45.0	50.0	1.00
Mean duration of having urticaria, weeks	69.4 (45.8)	74.8 (45.6)	0.78
Baseline score of overall severity	3.6 (0.8)	3.4 (0.7)	0.36
Baseline score of severity of pruritus	3.1 (0.5)	3.4 (0.6)	0.12
Baseline score of severity of erythema	3.0 (0.6)	3.1 (0.6)	0.51

Values in parentheses are standard deviations.

of urticaria, and their complete blood count, urine, and glucose levels were analyzed before initiating the therapy. This study was approved by the Ethics Committee at Kyoto University Graduate School of Medicine, and informed consent was obtained from each participant for this study.

All medications, including antihistamines, were stopped 1 week prior to the study. Forty patients were randomly assigned into 2 groups: group 1 with 20 patients who were initially treated with 5 mg olopatadine twice daily during the first period (days 1–7) and then switched to 60 mg fexofenadine twice daily during the second period (days 8–14), and group 2 with 20 patients who were initially treated with 60 mg fexofenadine twice daily during the first period and then switched to 5 mg olopatadine during the second period.

The outcomes were evaluated by patient-perceived improvement in the severity of pruritus, the severity of erythema, and the overall severity of urticaria. The severity of pruritus, erythema, and urticaria was evaluated using a numeric rating scale at baseline, on day 7, and day 14. The numeric rating scale score of severity was graded from 0 (none) to 4 (severe). Based upon the median of each variable representing the severity of pruritus, urticaria, and erythema, we categorized the score as ‘improved’ when more than 2 points were improved on days 7 and 14 compared to the baseline.

Log-binomial regression using generalized estimating equations was employed to evaluate the effectiveness of olopatadine versus fexofenadine on CIU by taking into account the period effect in each patient. The carryover effect was evaluated by comparing the change of scores after olopatadine versus fexofenadine use between group 1 and group 2, using Mann-Whitney test. χ^2 test was used for categorical univariate analysis. McNemar’s test was used to compare paired proportions. All analyses were performed using STATA version 11.2 (StataCorp LP, College Station, Tex., USA).

Results

The baseline characteristics are shown in table 1. Remarkable biases were not observed between group 1 and group 2. The results suggest that 70.0% of patients treated

with olopatadine during the first period showed improvement in the severity of urticaria on day 7, while 35.0% with fexofenadine during the first period showed improvement on day 7 (fig. 1). No carryover effects were observed in the effectiveness of each drug on the overall severity of urticaria ($p = 0.84$).

Log-binomial regression using generalized estimating equations revealed that olopatadine use was significantly associated with a larger improvement in the severity of pruritus [proportion ratio (PR) = 2.83, 95% confidence interval (CI) 1.76–4.56, $p < 0.001$], urticaria (PR = 2.24, 95% CI 1.39–3.58, $p = 0.001$), and erythema (PR = 2.79, 95% CI 1.66–4.72, $p < 0.001$; table 2).

As for the incidence and degree of the adverse effects, such as sleepiness and impaired performance, from each antihistamine, the olopatadine group had a tendency toward drowsiness (3 people) compared with the fexofenadine group (1 person). However, there was no significant difference in drowsiness between these 2 groups.

Discussion

CIU is occasionally difficult to control, and the skin lesions recur over months or years. H_1 antihistamines are the first choice to be considered when treating patients with CIU. There is no study comparing the therapeutic efficacies between olopatadine and other H_1 antihistamines in the treatment of CIU. In this study, we found that olopatadine was effective in reducing urticaria symptoms, such as erythema, wheal, and pruritus. This differential effect on urticaria suggests that olopatadine may possess a high affinity to the histamine receptor H_1 compared to other drugs. It has been reported that olopa-

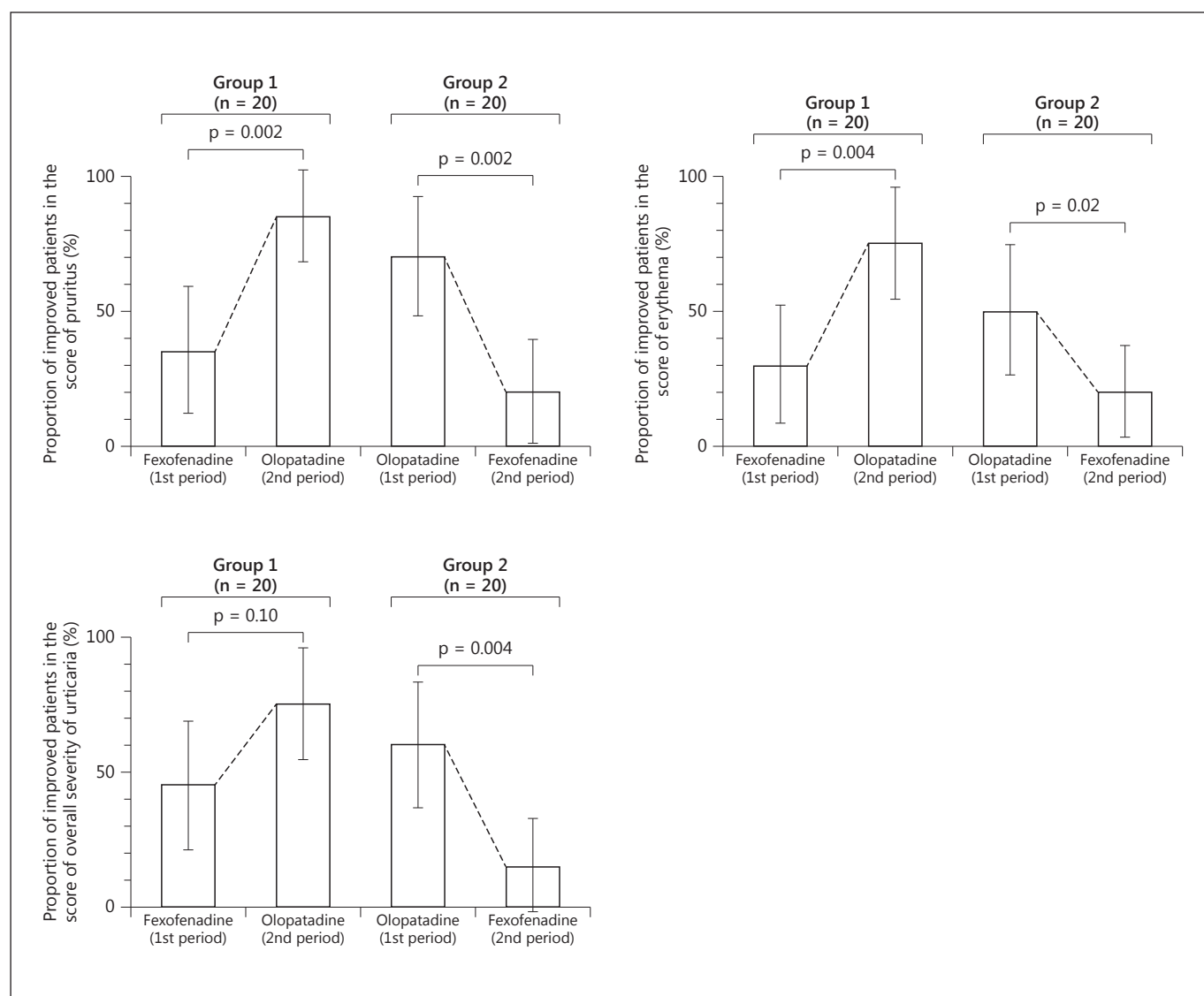


Fig. 1. Clinical evaluations of CIU treated with olopatadine versus fexofenadine. Forty patients with CIU were randomly assigned into 2 groups: group 1 with 20 patients who were initially treated with olopatadine and switched to fexofenadine, and group 2 with 20 patients who were initially treated with fexofenadine and then switched to olopatadine. The outcomes were evaluated for pruritus (top left panel), urticaria (bottom panel), and erythema (top right panel). We categorized a score as ‘improved’ when more than 2 points were improved on days 7 and 14 compared to the baseline. Error bars denote 95% CI.

Table 2. The PR of presenting a larger improvement in the severity of pruritus, estimated by the log-binomial regression analyses using generalized estimating equations

Characteristic	PR	95% CI	p value
Oropatadine use (vs. fexofenadine use)	2.83	1.76–4.56	<0.001
Period effect	1.08	0.82–1.41	0.60

dine is the only second-generation compound in which the carboxyl moiety does not interfere with phosphate binding, resulting in increased thermal stability of the H₁ receptor-olopatadine complexes [9].

Although there is the limitation that our study was not performed in a double-blind, placebo-controlled manner, the present findings suggest that olopatadine is a good candidate for the treatment of CIU.

References

- 1 Tokura Y, Kobayashi M, Kabashima K: Epidermal chemokines and modulation by antihistamines, antibiotics and antifungals. *Exp Dermatol* 2008;17:81–90.
- 2 Monroe EW: Nonsedating H₁ antihistamines in chronic urticaria. *Ann Allergy* 1993;71:585–591.
- 3 del Cuvillo A, Mullol J, Bartra J, Davila I, Jaurgui I, Montoro J, Sastre J, Valero AL: Comparative pharmacology of the H₁ antihistamines. *J Investig Allergol Clin Immunol* 2006;16(suppl 1):3–12.
- 4 Morita K, Koga T, Moroi Y, Urabe K, Furue M: Rapid effects of olopatadine hydrochloride on the histamine-induced skin responses. *J Dermatol* 2002;29:709–712.
- 5 Ohmori K, Hayashi K, Kaise T, Ohshima E, Kobayashi S, Yamazaki T, Mukouyama A: Pharmacological, pharmacokinetic and clinical properties of olopatadine hydrochloride, a new antiallergic drug. *Jpn J Pharmacol* 2002;88:379–397.
- 6 Handa S, Dogra S, Kumar B: Comparative efficacy of cetirizine and fexofenadine in the treatment of chronic idiopathic urticaria. *J Dermatolog Treat* 2004;15:55–57.
- 7 Purohit A, Melac M, Pauli G, Frossard N: Comparative activity of cetirizine and desloratadine on histamine-induced wheal-and-flare responses during 24 h. *Ann Allergy Asthma Immunol* 2004;92:635–640.
- 8 Tanizaki H, Ikoma A, Fukuoka M, Miyachi Y, Kabashima K: Effects of bepotastine and fexofenadine on histamine-induced flare, wheal and itch. *Int Arch Allergy Immunol* 2012;158:191–195.
- 9 Shimamura T, Shiroishi M, Weyand S, Tsujimoto H, Winter G, Katritch V, Abagyan R, Cherezov V, Liu W, Han GW, Kobayashi T, Stevens RC, Iwata S: Structure of the human histamine H₁ receptor complex with doxepin. *Nature* 2011;475:65–70.

Copyright: S. Karger AG, Basel 2015. Reproduced with the permission of S. Karger AG, Basel. Further reproduction or distribution (electronic or otherwise) is prohibited without permission from the copyright holder.