The effect of desloratadine on patch test reactions in Chinese patients

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Summary

Background: **Few data on the effect of antihistamines on patch test results in Chinese patients are currently available.**

Objectives: **To evaluate the effect of desloratadine on patch test reactions.**

Methods: **Patients known to have at least one strongly positive (+ +) test with an allergen were re-patch tested after 14 to 70 days (average time interval 26.3 days) of administering oral desloratadine 5 mg twice a day for 5 days before and during the test. Patch testing was performed with the previously recognized allergen according to the guidelines of the ICDRG. The − to + + + system was converted into numeric values (0, 1, 2, 3, 4) for statistic evaluation.**

Results: **Of the 58 chambers (47 patients), which were all strongly positive (+ +) during the 1st patch test, the situation was unchanged in 51 chambers; 4 + reactions and 2 + + + reactions were observed; and 1 chamber was negative. There was no statistically significant difference when comparing the scores of the 1st assessment with those of the 2nd ($p = 0.206$). If the patch test reaction of the patient who dropped out of the trial had changed from strongly positive (+ +) to negative, there would still have been no statistically significant difference between the score of the 1st assessment with those of the 2nd ($p = 0.107$).**

Conclusions: **The reaction of a patch test is not hampered by doubling dose of desloratadine. The anti-inflammatory effects of desloratadine on patch test reaction may be limited.** ***(Asian Pac J Allergy Immunol 2012;30:209-13)***

Key words: *desloratadine, patch test, anti-inflammatory effect, antihistamine, Chinese*

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Introduction

Patients with a more or less acute allergic contact dermatitis are often treated with steroids or antihistamines, sometimes for quite long periods. Patch tests are often performed in order to discover the cause of the contact dermatitis and the question then arises as to whether or not they should be done during the administration of such drugs, or postponed until treatment has been completed. Traditionally, antihistamine (H1 receptor antagonist) treatments are stopped 3 days before and during the patch test and glucocorticoids are avoided for 2 weeks before and during the test.[1] Dermatologists usually feel uncomfortable about testing patients under treatment with antihistamines and prefer to delay testing until antihistamines have been stopped. Li et al. designed a double-blind, placebo-controlled, randomized, study of 121 patients in which they did not find any difference in the patch reaction after loratadine in the conventional dose.[2] It has been recognized for some years that in addition to being potent antihistamines - a number of the second-generation drugs appear to possess several anti-allergic effects that cannot be explained by antagonism of the H1 receptor.[3] Desloratadine, a new-generation antihistamine, is a potent antihistamine H1[4] which displays several interesting anti-allergic and anti-inflammatory properties,[5] especially in high doses.[6-9] Previous studies[2,10,11] mainly focused on the antihistaminic effects of antihistamines on patch test reactions and may have neglected the anti-inflammatory effects. The objective of our study was to determine whether the anti-inflammatory effects of a new-generation antihistamine, Desloratadine, can suppress the reactions of patch testing or not. Desloratadine was

chosen to further research the anti-inflammatory effects of antihistamines on patch test reaction.

Methods

Subjects

The patients were recruited from February to August in 2011 in the departments of dermatology at the Second Affiliated Hospital of Soochow University and Suzhou Hospital Affiliated to Nanjing Medical University.

To be included, they had to have at least one positive test showing + + with an allergen from the Chinese standard series of contact allergens at 72 hours according to the International Contact Dermatitis Research Group (ICDRG)[12] scale. It is well known among experienced patch testers,[13,14] + reactions do not always indicate allergy. The + + + reactions are too intense for these patients to accept repeat patch testing. Eleven males and 37 females (Table 1) with a mean age ± SD of 36.1 ± 12.9 years were enrolled in the trial after they had given written informed consent. Exclusion criteria were the following: atopic patients according to clinical history (absence of asthma, allergic rhinitis or conjunctivitis and atopic dermatitis), patients with an eczema on the back (no possibility of retesting), patients with a severe organ deficiency, patients allergic to desloratadine, piperidines and other components of desloratadine pills, patients under treatment with topical corticosteroids at the test site within the last 4 weeks, systemic corticosteroids in the last 8 weeks, or immunomodulator agents in the last 1 week, and patients whose back had been under insolation or exposed to UVB in the last 4 weeks.

The research protocol was approved by the Ethics Committees of the Second Affiliated Hospital of Soochow University and Suzhou Hospital, affiliated to Nanjing Medical University.

Patch test

The patch test contains 20 standard allergens in IQ chambers (Chemotechnique Diagnostics AB, Sweden).

The patch test was positioned symmetrically on the back. Patch tests were removed after 48 hours; the results read after 72 hours using the ICDRG clinical recording method. Clinical assessment of the intensity of the reaction was carried out according to the recording system of ICDRG: − negative, +? doubtful reaction (faint erythema), + weak positive (erythema, infiltration, possibly papules), + + strong positive reaction (erythema, infiltration, papules, vesicles), + + + extreme positive reaction (intense erythema, infiltration, coalescing vesicles). Clinical assessment was carried out by the same technician.

Table 1. 20 standard allergens

Allergens	Concentration (%)
Cobalt chloride	1.0 in petrolatum base
Mercapto mix	2.0 in petrolatum base
Imidazolidinylurea	2.0 in petrolatum base
4-Phenylenediamine base	1.0 in petrolatum base
N-(Cyclohexylthio) phthalimide	1.0 in petrolatum base
Potassium dichromate	0.5 in petrolatum base
Ethylenediamine dihydrochloride	1.0 in petrolatum base
Colophony	20.0 in petrolatum base
Formaldehyde	1.0 in aqueous base
Epoxy resin	1.0 in petrolatum base
2-Bromo-2-nitropropane-1,3-diol	0.25 in petrolatum base
Thiuram mix	1.0 in petrolatum base
Parabens	16.0 in petrolatum base
Nickel sulfate	5.0 in petrolatum base
Sesquiterpene lactone mix	0.1 in petrolatum base
Fragrance mix	8.0 in petrolatum base
Cl + Me – isothiazolinone	0.01 in aqueous base
Black rubber mix	0.6 in petrolatum base
Carba mix	3.0 in petrolatum base
Quarternium 15	1.0 in petrolatum base

Intervention

The patients were re-patch tested after 14 to 70 days (average time interval 26.3 days) of administering oral desloratadine 5 mg twice a day for 5 days before and during the test. Patch testing was performed with the previously recognized allergen according to the guidelines of the ICDRG.

There are 5 mg of desloratadine in each pill. The desloratadine pills are made in Hangzhou Merck Sharp & Dohme Pharmaceutical Company Limited.

Evaluation

The − to + + + system was converted into numeric values (0, 1, 2, 3, 4) for statistic evaluation.

Data analysis

The results were analyzed by Wilcoxon Matched-Pairs Signed-Ranks Test using SPSS17.0 software. We hypothesized that the use of desloratadine 5 mg twice a day would significantly

reduce intensity of patch test reactions with 2-tailed $P < 0.05$.

Result

One patient did not complete the trial complaining of severe sleepiness after the first pill of desloratadine. This patient was strongly positive (+ +) to nickel sulfate in the 1st patch testing. Of the 47 patients who completed the research, 58 chambers (13 allergens) were found to be strongly positive (+ +) during the 1st patch test.

Of the 58 chambers (47 patients), which were all strongly positive (+ +) during the 1st patch test, the situation was unchanged in 51 chambers; 4 had + reactions in two chambers containing Cl + Me - isothiazolinone, one containing 4-Phenylenediamine base and one containing Nickel sulfate） and 2 + + + reactions were observed (one due to Sesquiterpene lactone mix and the other one to Fragrance mix); and 1 chamber containing（Carba mix）was negative (Table 2). Using the Wilcoxon matched-pairs signed-ranks test, the integral patch test [Mean Rank (-) = 4.20, Mean Rank (+) = 3.50, Z= -1.265, 2-tailed P = 0.206] and the nickel sulfate patch test [Mean Rank (-) = 1.00, Mean Rank (+) = 0, Z= -1.000, 2-tailed P = 0.317] had good symmetry, and there was no statistically significant difference between the scores. The scores of the formaldehyde patch test were the same at the 1st and the 2nd assessments.

Despite the fact that the patch test reaction of one patient changed from strongly positive (+ +) to negative, there was still no statistically significant difference between the score of the 1st assessment and those of the 2nd. The results of statistical analysis are as follows: the integral patch test [Mean Rank (-) = 4.83, (Mean Rank (+) = 3.50, Z= -1.613, 2-tailed P = 0.107], and the nickel sulfate patch test [Mean Rank (-) = 1.50, Mean Rank (+) = 0, Z= -1.342, 2-tailed P = 0.180].

Table 2. Results of 1st and 2nd patch tests

Results of patch test	1st (N)	2nd (N)			
	++	—	+	++	+++
Nickel sulfate	23	0	1	22	0
Formaldehyde	12	0	0	12	0
Fragrance mix	4	0	0	3	1
Potassium dichromate	4	0	0	4	0
Colophony	5	0	0	5	0
4-Phenylenediamine base	2	0	1	1	0
Cl + Me – isothiazolinone	2	0	2	0	0
Ethylenediamine dihydrochloride	1	0	0	1	0
Cobalt chloride	1	0	0	1	0
Thiuram mix	1	0	0	1	0
Parabens	1	0	0	1	0
Sesquiterpene lactone mix	1	0	0	0	1
Carba mix	1	1	0	0	0

Discussion

Desloratadine is a new-generation antihistaminic compound and is the primary active metabolite of loratadine. Desloratadine is a potent antihistamine H1 which displays several interesting anti-allergic and anti-inflammatory properties.[5] Many of the reported anti-inflammatory effects of desloratadine are seen with higher than standard doses in experimental settings.[6-9] Desloratadine may exert effects on eosinophil chemo-attractants, precursors, activation, and survival. Ten mg of desloratadine down-regulates eosinophil recruiting chemokines in peripheral blood mononuclear cells of allergic patients induced by an allergen in atopic patients.[15] In vitro, desloratadine also inhibits the generation of histamine and leukotriene (LT) C4 release by human basophils.[16] Human mast and basophilic cells exposed to desloratadine show reduced production of cytokines central to inflammatory responses.[17]

Whether or not treatments must be stopped before testing is a matter of debate.[10] Grob J.J. et al. did not find any difference in the patch test reaction after

cetirizine in a double-blind, placebo-controlled, randomized, cross-over pilot study (by clinical recording and the standardized chromatometry). A group of 27 patients with a positive patch test to an allergen alternatively received cetirizine 10 mg OD or placebo during a 14-day period. At day 11 of each period, patch testing was performed with the allergen. The image analysis showed a skin reaction significantly reduced under cetirizine (p = 0.03), but the clinical recording and the standardized chromatometry did not show any difference between groups. Motolese et al. reported that loratadine, an antihistamine with other anti-inflammatory effects, reduced the patch test reaction in a study of 18 patients (by clinically and echographic evaluation). Echographic evaluation of patch test reactions was carried out using a 20 MHz B scanner (Dermascan C, Cortex Technology).[11] Scans were stored on disks and elaborated by software for image analysis, which ascribes a numerical scale (ranging from 0 to 255) to the echoes' amplitude levels, enabling

calculation of extension of areas reflecting within the chosen amplitude interval. Extension of 0-30 areas, measured in number of pixels, is proportional to the intensity of the eczematous reaction. Patients were re-patch tested after administering oral loratadine 10 mg per day for 4 days before and during the test. The mean clinical score and mean extension of per patch test was significantly lower at re-patch testing than in the 1st series. Compared with clinically evaluation, echographic evaluation did not show any superiority. There were conflicts between these two small sample studies. So Li et al. designed a double-blind, placebo-controlled, randomized study in which they did not find any difference in the patch test reaction after loratadine.[2] One hundred twenty one patients with a positive patch test to nickel sulfate were randomized into two groups, one group of 61 patients received loratadine 10 mg daily and another received placebo daily during a 14-day period. The patch test was applied at day 11 and clinical evaluaton of patch test was conducted at day 14. Fifty five patients in the experimental group and 53 patients in control group showed positive reactions as before, and there was no significant difference between the two groups. Previous studies mainly focused on the antihistaminic effects of antihistamines in conventional dose. Considering the anti-inflammatory effects of antihistamines in conventional doses may be limited, so we double the dose of desloratadine while re-patch testing in our study. The results further confirm the conclusion that the antihistamine characteristics of antihistamines have no effect on patch test reactions and demonstrates the anti-inflammatory effects of desloratadine in high-dose can not suppress patch test reaction.

Nickel has been shown to be one of the most reproducible patch test allergens when a patient is rechallenged,[18] so only nickel-allergic patients were included in most of the previous studies. In our study, of the 23 chambers showed strongly positive (+ +) reactions to Nickel sulfate allergen during the 1st patch test and only one chamber changed from strongly positive (+ +) to positive (+) reaction at the second test. It can also be concluded from our study that nickel allergy is probably a robust and reliable model to assess the effect of a drug. However, it is different from the previous studies, in that our study contains a variety of allergens. It is more representative than the previous studies which only used nickel sulfate allergen. In our study, the reactions to Formaldehyde, Potassium dichromate and Colophony patch tests remained the same during the 2nd patch test. Formaldehyde, Potassium dichromate and Colophony allergies may also be stable.

Two factors need to be considered in the interpretation of our results. First, we chose only patients with + + reaction during the 1st patch test. We need to research any degree of reaction in the results, including + and + + + reaction groups. Second, the time interval between the test sessions was variable. The shortest session in this study is 14 days and the longest session is 70 days. A climatic change between the first and the second period may affect the patch test reaction.[10]

In our study, the patients were re-patch tested after administering a doubling dose of desloratadine. The results of the study show that the reaction of a patch test is not hampered by high-dose desloratadine and the anti-inflammatory effects of high-dose desloratadine on patch test reaction may be subtle. Therefore, there is no need to stop antihistamines or delay testing in patients under antihistamine treatment. This may facilitate patient testing in daily practice. The dose of desloratadine used in this study, 10 mg daily, is higher than the usual prescription dose of 5 mg daily. A dose of 20 mg daily has previously been shown to be safe and effective. Up-titration of dose to as high as 4 times the starting dose has been advocated in international guidelines to surmount the often relative unresponsiveness to traditional doses of antihistamines in urticaria.[19,20]

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