

Comparative efficacy of levocetirizine, desloratidine and fexofenadine by histamine wheal suppression test

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ABSTRACT

Background: Histamine is the major mediator of allergic reactions. Newer H1 antihistaminics like levocetirizine, fexofenadine, and desloratidine are used in the treatment of seasonal and perennial allergic rhinitis and urticaria. The ability to block the cutaneous response to intradermal histamine is used to evaluate the potential of antihistamines. **Aims:** To compare the potency, onset, and duration of action of the commonly used antihistamines-levocetirizine, fexofenadine, and desloratidine. **Methods:** Thirty volunteers were given three single doses of levocetirizine, fexofenadine and desloratidine at weekly intervals. A pretest was performed by using the intradermal histamine prick test. After administration of the drugs, the intradermal test was repeated at ½, 1, 2, 3, 6 and 24 h, and the sizes of the wheal were measured. The mean values were taken and were compared by using Levene's t-test. **Results:** At 30 min, fexofenadine showed a statistically significant suppression of wheal size compared to levocetirizine and desloratidine. Two and three hours after administration, levocetirizine and fexofenadine showed statistically significant inhibition of wheal size while only levocetirizine had this effect after six hours when compared to desloratidine. Desloratidine showed greater inhibition of wheal size at the end of 24 h when compared to levocetirizine and fexofenadine but this was not statistically significant. **Conclusions:** Fexofenadine had the earliest onset of action while levocetirizine showed maximum inhibition of wheal response after three and six hours.

Key Words: Antihistamine, Prick test

INTRODUCTION

Histamine is the major mediator of allergic reactions and acts mainly through the histamine receptors, H1 and H2 found in cutaneous blood vessels and H3 in the brain.^[1] Antihistamines are drugs which block H1 receptors and suppress the wheal and flare reaction caused by histamine. Levocetirizine, fexofenadine and desloratidine are second generation antihistamines that are commonly used in the treatment of urticaria and perennial allergic rhinitis. The potency of an antihistamine is assessed by its ability to block the wheal and flare reaction.^[2] We have conducted a study to compare the onset and potency of levocetirizine, fexofenadine and desloratidine by using the histamine wheal suppression test.

METHODS

This study was done on 30 healthy volunteers (18-50 years of age) after obtaining their informed consent. The volunteers were not taking any antihistamines, steroids or immunosuppressants for seven days prior to the study. None of them had any history of atopy, drug hypersensitivity or use of alcohol. Pregnant and lactating women were excluded.

Volunteers were administered levocetirizine 5 mg, desloratidine 5 mg and fexofenadine 180 mg at weekly intervals to prevent any carryover effect of the drugs. Levocetirizine was administered in the 1st week, desloratidine in the 2nd week and fexofenadine in the 3rd week. A prick test was performed before the administration

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of each drug and after ½, 1, 2, 3, 6, 24 hours following the administration of the drug. The test was performed in a marked square area of 1 x 1 cm at different sites each time, on the flexor aspect of the forearm. The size of the histamine-induced wheal was recorded each time.

A drop of 0.1% w/v of histamine solution was placed on the flexor aspect of the forearm. The skin was pricked through the histamine solution with a lancet. The tip of lancet was kept parallel to the skin surface and the skin lifted by tenting by the lancet at an angle of 45-60°.

After one minute, the test site was wiped with filter paper to remove the excess histamine solution. The size of the wheal was calculated by measuring the maximum diameter of the wheal and the orthogonal diameter with a transparent scale after ten minutes.

The readings were analyzed statistically by applying the Levene's T test for comparison of drugs. A *P* value of 0.05 was considered to be statistically significant.

RESULTS

The mean values of wheal sizes in response to intradermal histamine challenge for levocetirizine 5 mg, desloratadine 5 mg and fexofenadine 180 mg after ½, 1, 2, 3, 6, 24 hours following drug administration are shown in Table 1.

Half an hour after administration, fexofenadine showed a statistically significant suppression of wheal size compared to levocetirizine (*P* = 0.040) and desloratadine (*P* = 0.036).

However, after one hour, all the three drugs showed a decrease in wheal size that was not statistically significant.

After two and three hours, levocetirizine (*P* = 0.000) and fexofenadine (*P* = 0.000) showed a statistically significant inhibition of wheal size when compared to desloratadine.

Only levocetirizine showed a statistically significant inhibition of wheal response after six hours (*P* = 0.24), while all three drugs showed substantial (but not statistically significant) reduction in wheal size (*P* > 0.05).

DISCUSSION

Statistical analysis of the results showed that fexofenadine has an early onset of action (after half an hour) as compared to levocetirizine and causes a significantly higher reduction of wheal size after three and six hours when compared to desloratadine. A study by Simons and Simons showed that fexofenadine had a more rapid onset of inhibition for cutaneous whealing after histamine challenge compared to loratidine.^[3] In our study, the mean suppression by desloratadine was maximum at 24 hours but this value was not statistically significant when compared with that by fexofenadine and desloratadine.

Fexofenadine is a second generation antihistamine and is an active metabolite of terfenadine.^[4] Fexofenadine is readily absorbed via the oral route with peak plasma levels at 1-3 h after administration and an elimination half-life of 11-15 h.^[4] Fexofenadine has been shown to have a faster onset of flare suppression than desloratadine (one vs five hours) and an equally rapid onset of wheal suppression suggesting increased *in vivo* H1 receptor antagonist potency.^[5]

In our study, the wheal suppression by fexofenadine was superior to that by levocetirizine and desloratadine after half an hour following drug administration.

Fexofenadine also showed significant wheal suppression after two and three hours when compared to desloratadine.

Levocetirizine is an active enantiomer of cetirizine with an onset of action at about one hour and an elimination half-life of seven hours.^[6] It has been compared with other antihistamines like fexofenadine and desloratadine and has been found to have an efficacy that exceeded that of loratidine.^[2] Levocetirizine was found to be more effective than desloratadine in inhibiting wheal and flare responses to histamine in human skin *in vivo*, with 1.25 mg levocetirizine being more effective than 10 mg desloratadine.^[7]

In our study also, levocetirizine showed a significant wheal suppression after two, three and six hours when compared to desloratadine.

Table 1: Mean of wheal suppression in mm

| | Pretest | ½ h | 1 h | 2 h | 3 h | 6 h | 24 h |
|----------------|---------|--------|--------|--------|--------|--------|--------|
| Levocetirizine | 5.0690 | 4.7241 | 3.7586 | 2.5172 | 1.5172 | 1.9655 | 2.9655 |
| Fexofenadine | 5.2333 | 4.3000 | 3.6000 | 2.2333 | 1.5000 | 2.1333 | 3.1667 |
| Desloratadine | 5.0968 | 4.7097 | 4.0323 | 3.3871 | 2.5484 | 2.5484 | 2.8387 |

Desloratadine is another newer antihistamine that is a biologically active metabolite of loratadine.^[8] It is found to be more potent than loratadine and attains the maximum plasma concentration at 2.5 h after administration with a mean elimination half life of 17 hours.^[8]

Desloratadine has been found to be less efficacious than fexofenadine and levocetirizine in various other studies.^[9] In the current study, wheal suppression by desloratadine was less than that by levocetirizine and fexofenadine.

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