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Cochrane Database of Systematic Reviews 2014, Issue 11. Art. No.: CD006137.
DOI: 10.1002/14651858.CD006137.pub2.

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[Intervention Review]

H1-antihistamines for chronic spontaneous urticaria

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Editorial group: Cochrane Skin Group.
Publication status and date: Edited (no change to conclusions), published in Issue 5, 2017.

Citation: Sharma M, Bennett C, Cohen SN, Carter B. H1-antihistamines for chronic spontaneous urticaria. *Cochrane Database of Systematic Reviews* 2014, Issue 11. Art. No.: CD006137. DOI: 10.1002/14651858.CD006137.pub2.

ABSTRACT

Background

Chronic spontaneous urticaria (CSU) is characterised by the development of crops of red, itchy, raised weals or hives with no identifiable external cause.

Objectives

To assess the effects of H1-antihistamines for CSU.

Search methods

We searched the following databases up to June 2014: Cochrane Skin Group Specialised Register, CENTRAL (2014, Issue 5), MEDLINE (from 1946), EMBASE (from 1974) and PsycINFO (from 1806). We searched five trials registers and checked articles for references to relevant randomised controlled trials.

Selection criteria

We included randomised controlled trials of H1-antihistamines for CSU. Interventions included single therapy or a combination of H1-antihistamines compared with no treatment (placebo) or another active pharmacological compound at any dose.

Data collection and analysis

We used standard methodological procedures as expected by The Cochrane Collaboration.

Our primary outcome measures were proportion of participants with complete suppression of urticaria: 'good or excellent' response, 50% or greater improvement in quality of life measures, and adverse events. We present risk ratios (RR) with 95% confidence intervals (CIs).

Main results

We identified 73 studies (9759 participants); 34 studies provided data for 23 comparisons. The duration of the intervention was up to two weeks (short-term) or longer than two weeks and up to three months (intermediate-term).

Cetirizine 10 mg once daily in the short term and in the intermediate term led to complete suppression of urticaria by more participants than was seen with placebo (RR 2.72, 95% CI 1.51 to 4.91). For this same outcome, comparison of desloratadine versus placebo in the

intermediate term (5 mg) (RR 37.00, 95% CI 2.31 to 593.70) and in the short term (20 mg) (RR 15.97, 95% CI 1.04 to 245.04) favoured desloratadine, but no differences were seen between 5 mg and 10 mg for short-term treatment.

Levocetirizine 20 mg per day (short-term) was more effective for complete suppression of urticaria compared with placebo (RR 20.87, 95% CI 1.37 to 317.60), and at 5 mg was effective in the intermediate term (RR 52.88, 95% CI 3.31 to 843.81) but not in the short term, nor was 10 mg effective in the short term.

Rupatadine at 10 mg and 20 mg in the intermediate term achieved a 'good or excellent response' compared with placebo (RR 1.35, 95% CI 1.03 to 1.77).

Loratadine (10 mg) versus placebo (RR 1.86, 95% CI 0.91 to 3.79) and loratadine (10 mg) versus cetirizine (10 mg) (RR 1.05, 95% CI 0.76 to 1.43) over short-term and intermediate-term treatment showed no significant difference for 'good or excellent response' or for complete suppression of urticaria, respectively.

Loratadine (10 mg) versus desloratadine (5 mg) (intermediate-term) showed no statistically significant difference for complete suppression of urticaria (RR 0.91, 95% CI 0.78 to 1.06) or for 'good or excellent response' (RR 1.04, 95% CI 0.64 to 1.71). For loratadine (10 mg) versus mizolastine (10 mg) (intermediate-term), no statistically significant difference was seen for complete suppression of urticaria (RR 0.86, 95% CI 0.64 to 1.16) or for 'good or excellent response' (RR 0.88, 95% CI 0.55 to 1.42).

Loratadine (10 mg) versus emedastine (2 mg) (intermediate-term) showed no statistically significant difference for complete suppression (RR 1.04, 95% CI 0.78 to 1.39) or for 'good or excellent response' (RR 1.09, 95% CI 0.96 to 1.24); the quality of the evidence was moderate for this comparison.

No difference in short-term treatment was noted between loratadine (10 mg) and hydroxyzine (25 mg) in terms of complete suppression (RR 1.00, 95% CI 0.32 to 3.10).

When desloratadine (5 to 20 mg) was compared with levocetirizine (5 to 20 mg), levocetirizine appeared to be the more effective (P value < 0.02).

In a comparison of fexofenadine versus cetirizine, more participants in the cetirizine group showed complete suppression of urticaria (P value < 0.001).

Adverse events leading to withdrawals were not significantly different in the following comparisons: cetirizine versus placebo at 10 mg and 20 mg (RR 3.00, 95% CI 0.68 to 13.22); desloratadine 5 mg versus placebo (RR 1.46, 95% CI 0.42 to 5.10); loratadine 10 mg versus mizolastine 10 mg (RR 0.38, 95% CI 0.04 to 3.60); loratadine 10 mg versus emedastine 2 mg (RR 1.09, 95% CI 0.07 to 17.14); cetirizine 10 mg versus hydroxyzine 25 mg (RR 0.78, 95% CI 0.25 to 2.45); and hydroxyzine 25 mg versus placebo (RR 3.64, 95% CI 0.77 to 17.23), all intermediate term.

No difference was seen between loratadine 10 mg versus mizolastine 10 mg in the proportion of participants with at least 50% improvement in quality of life (RR 3.21, 95% CI 0.32 to 32.33).

Authors' conclusions

Although the results of our review indicate that at standard doses of treatment, several antihistamines are effective when compared with placebo, all results were gathered from a few studies or, in some cases, from single-study estimates. The quality of the evidence was affected by the small number of studies in each comparison and the small sample size for many of the outcomes, prompting us to downgrade the quality of evidence for imprecision (unless stated for each comparison, the quality of the evidence was low).

No single H1-antihistamine stands out as most effective. Cetirizine at 10 mg once daily in the short term and in the intermediate term was found to be effective in completely suppressing urticaria. Evidence is limited for desloratadine given at 5 mg once daily in the intermediate term and at 20 mg in the short term. Levocetirizine at 5 mg in the intermediate but not short term was effective for complete suppression. Levocetirizine 20 mg was effective in the short term, but 10 mg was not. No difference in rates of withdrawal due to adverse events was noted between active and placebo groups. Evidence for improvement in quality of life was insufficient.

PLAIN LANGUAGE SUMMARY

H1-antihistamines for chronic spontaneous urticaria

Background

Chronic spontaneous urticaria (CSU) is a condition characterised by a rash of red itchy raised weals or hives, which appear for no identifiable reason. Other names include chronic idiopathic or chronic ordinary urticaria. 'Spontaneous' differentiates this type of urticaria from 'inducible' or 'physical' urticaria, for which there are specific triggers such as cold or pressure. 'Chronic' indicates that the condition has continued for at least six weeks. Hives may be intensely itchy, and the appearance may be unsightly and distressing to sufferers. In some cases, hives can be accompanied by deeper swelling, known as angio-oedema, which is most common around the eyes and mouth.

Antihistamine drugs, specifically H1 antihistamines, are the mainstay of treatment for urticaria, although they control the condition rather than cure it. Many antihistamines are available to buy without a prescription, including brand names such as Clarityn, Piriton, Zirtek, Benadryl and Phenergan (brand names may differ by country).

Review question

Which H1-antihistamines are effective and safe for CSU?

Study characteristics

We included 73 randomised controlled trials, with 9759 participants of all ages and looked for complete suppression of urticaria. The duration of the intervention was up to two weeks (short-term) or longer than two weeks and up to three months (intermediate-term).

Key results

We investigated clinical trials in which one therapy was compared against another or against placebo (direct comparisons). We found that for general use, 10 mg once daily of cetirizine for short-term and intermediate-term duration was effective in completely suppressing urticaria, although not in all individuals. Some benefit may be associated with use of desloratadine at 5 mg for at least an intermediate term and at 20 mg in the short term. Levocetirizine at 5 mg was effective for complete suppression in the intermediate term but not in the short term. A higher dose of 20 mg was effective in the short term, but 10 mg was not.

Adverse events, such as headache or dry mouth, are tolerable with most antihistamines. Evidence is less clear for improvement in quality of life (e.g. reduction in sleep disturbance from itching, less distress from the appearance of hives) as many studies did not address this.

We cannot say whether one antihistamine works better than all the rest, as we did not have head-to-head evidence for every possible treatment comparison.

Quality of the evidence

The overall quality of the evidence found for most outcomes was low. Further well-designed and carefully reported comparative studies are required, if we are to find out how well these medicines work, and if any adverse effects are reported, especially over periods of up to several months.