

Cimetidine Increases the Plasma Concentration of Hydroxyzine

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The combination of hydroxyzine and cimetidine is reported to be more effective than hydroxyzine alone in chronic urticaria. The plasma concentration of hydroxyzine was studied in seven patients treated both with the hydroxyzine 25 mg t.i.d. and the combinations of hydroxyzine 25 mg and cimetidine 200 mg t.i.d. Hydroxyzine plasma concentrations were definitely higher during the combination treatment than during hydroxyzine alone. This may explain the effectiveness of the combination treatment. *Key word: Urticaria.* (Received August 23, 1985.)

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The combination of H1 and H2 antagonists has been claimed to be more effective in the treatment of chronic urticaria than H1 antagonist alone (1, 2). On the other hand, some double blind studies have shown that no such effect can be achieved (3, 4, 5). Cimetidine is known to inhibit microsomal drug metabolism (6, 7). This led us to study the effect of cimetidine on hydroxyzine blood concentrations in patients with chronic urticaria in whom the combination was tried as a symptomatic treatment.

PATIENTS AND METHODS

Seven patients hospitalized for chronic urticaria with severe daily symptoms were first treated with 25 mg hydroxyzine three times daily. On the second treatment day blood was drawn in the morning, at 2 pm and at 8 pm before the 25 mg dose of hydroxyzine was administered. On the third and fourth days 200 mg cimetidine was administered together with hydroxyzine. On the fourth day blood was drawn as on day 2.

Seven control patients were subjected to equal hydroxyzine treatment and equal blood sampling without cimetidine.

Hydroxyzine plasma concentrations were determined by capillary gas chromatography.

RESULTS

The hydroxyzine plasma concentrations of the patients during treatment with hydroxyzine alone and in combination with cimetidine are presented in Fig. 1. There was a wide inter-individual variation in the concentrations. The mean concentrations obtained during combination treatment with hydroxyzine and cimetidine are significantly higher than those obtained with hydroxyzine alone. An increase in the concentrations was obtained in six patients but in one patient cimetidine did not have any effect on hydroxyzine plasma concentration.

The mean hydroxyzine plasma concentrations of the control patients were 32.9 ± 3.8 , 55.6 ± 6.8 , 41.9 ± 4.0 and 31.1 ± 6.0 , 59.3 ± 8.9 , 40.7 ± 6.1 at 8, 14 and 20 h in the second and fourth days, respectively.

DISCUSSION

In a double blind study, Monroe et al. (2) have shown that the combination of cimetidine to hydroxyzine increases the therapeutic effect obtained in patients with chronic urticaria.

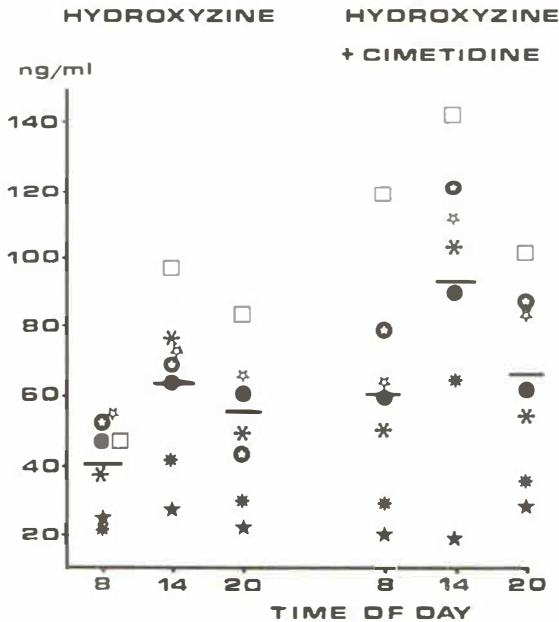


Fig. 1. Plasma concentrations of hydroxyzine in patients with chronic urticaria on the second day of treatment with hydroxyzine 25 mg t.i.d. and hydroxyzine 25 mg plus cimetidine 200 mg t.i.d. Different figures represent values obtained in individual patients and bars the mean concentrations. The difference between values with hydroxyzine alone and those with hydroxyzine plus cimetidine is highly significant ($p < 0.001$ —Student's *t*-test for paired observations).

On the other hand, the combination of cimetidine to chlorpheniramine has not been more effective than chlorpheniramine alone (3, 4, 5). The present results show that the combination of cimetidine to hydroxyzine causes a definite increase in the hydroxyzine plasma concentrations. This increase is possibly the reason why the combination treatment is in some patients more effective than hydroxyzine alone. A point against this assumption is presented in the study of Harvey & Schocket (7) who studied the effect of the same drug combination on histamine induced wheal formation. They state that the combination is more effective in reducing the wheal size than hydroxyzine alone and further that doubling the dose of hydroxyzine did not further reduce the wheal area. It is, however, probable that in urticaria the wheal formation requires other mediators in addition to histamine. Why, then, is the effect of chlorpheniramine not augmented by cimetidine? One possible explanation may be that it is not metabolized through the same liver enzymes as hydroxyzine.

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