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LETTER TO THE EDITOR

HYPOGLYCEMIC EFFECT OF TERFENADINE IN PATIENTS OF ALLERGIC RHINITIS

Sir,

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Antihistaminics are frequently prescribed for the relief of symptoms due to allergic rhinitis, acute coryza, rhinoconjuctivitis, urticaria and anaphylaxis. Second generation antihistaminics (astemizole and terfenadine, cetrizine, acrivastine, loratidine and azelastine) are preferred over 1st generation (chlorpheniramine, diphenhydramine, hydroxyzine, pyrilamine and promethazine) because of favorable risk benefit ratio with the former as compared to latter (1, 2).

Two of our patients who were prescribed terfenadine (60 mg twice daily) and astemizole (10 mg once daily) respectively, developed the symptoms of hypoglycemia, which was confirmed on blood glucose estimation. Though, terfenadine and astemizole have been reported to cause a wide variety of adverse reactions including increased appetite and fatal cardiovascular events (3-5), there is no report of their effects on blood glucose. We, therefore investigated the effect of terfenadine and astemizole on blood glucose in man.

The trial was conducted at the University College of Medical Sciences and G.T.B. Hospital, Delhi from July to December 1994. Newly diagnosed patients of allergic rhinitis were enrolled in the study, after informed written consent. Patients having diabetes mellitus, cardiovascular disease, respiratory illness, kidney disorder or liver disease were excluded from the study. The trial design was randomized, double blind, placebo controlled, single dummy, and parallel groups.

Terfenadine (60 mg twice daily), astemizole (10 mg, morning and astemizole dummy at evening) and matched placebo (twice daily) were used. Drugs were filled in capsules. Two different colours of identical capsules were used, one for morning doses (terfenadine, astemizole and placebo) and other for the evening doses (terfenadine, dummy astemizole and placebo). Seven days supply of drugs was given to patients. Compliance was checked by counting the left over capsules at each visit. No other drug was administered to any patient. Adverse drug reactions were enquired from the patients.

Blood glucose (fasting) was estimated by the method of 'glucose oxidase' (6), at basal level (before drug administration), and at acute drug administration (2.0 h after the morning dose on 1st day) and chronic administration (2 h after the morning dose on 7th day). Each time, the patients came overnight fasting (had a meal at 9 PM on the previous night) and the blood glucose was measured at 10.30 AM. Dietry habbits (calories intake, type and time of the meal) of the patients were controlled, 7 day prior and during the study period.

The data were analysed by Student's paired 't' test (for intra-group comparisons) and unpaired 't' test (for inter-group compairsons). The value of P less than 0.05 was considered as statistically significant.

Thirty patients, of age (20 to 50 yrs) and weight (45 to 70 kg) of either sex, presenting with allergic rhinitis were enrolled in the trial. No drop out occurred and all the patients were fully compliant to drugs.

The effect of acute and chronic administration of drugs is shown in Table I. There was no difference in the blood glucose at the basal level, in the three groups. However, acute and chronic administrations of terfenadine caused a significant fall in blood glucose level

TABLE I: Effect of acute and chronic administrations of placebo astemizole and terfenadine on blood glucose (g%). (Data are $\bar{X}$ ± SEM)

	Placebo (n=10)	*Astemizole (n=10)*	*Terfenadine (n=10)*
Basal	88.20 ± 4.63	86.50 ± 4.89	87.10 ± 4.63
Acute administration	89.80 ± 3.10	79.70 ± 5.05	79.00 ± 5.57*[a]
Chronic administration	87.40 ± 4.09	75.70 ± 3.16	71.70 ± 7.45**[a]

n = number of patients in each group; *P < 0.05; **P < 0.02 vs basal value; [a] = P < 0.05 vs placebo at respective intervals.

as compared to its basal reading (P < 0.05 and P < 0.02 respectively) and also as compared to placebo on acute and chronic dosings (P < 0.05 and P < 0.5 respectively). Similarly, the astemizole also caused a drop in blood glucose level as compared to its basal level and placebo on acute and chronic administrations, though the results were not statistcally significant. No other adverse drug reaction occured during the study.

From the present study, it is evident that acute or chronic use of terfenadine and astemizole may cause hypoglycemia. The three groups were almost homogenous in disease state and patient characteristics. No other drug was administered to any patient. The exact mechanism involved in the blood glucose lowering effects of these drugs in still unclear. However, antidiabetic, sulphonylurea produces a decrease in blood glucose by blocking the pancreas ATP potassium channel (7). Terfenadine has also been reported to block an outward (delayed) rectifier potassium channel in the heart, leading to the production of ventricular arrhythmias (4, 5). We hypothesize that terfenadine-induced hypoglycemia could be due to blockade of potassium channels in the pancreas. Further investigations are required to establish the exact mechanism of hypoglycemia.

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