The influence of cimetidine and ranitidine on the plasma lipid pattern

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The influence of H₂-receptor antagonist drugs on the plasma lipid pattern has been studied prospectively in 51 patients treated with cimetidine (26 patients) or ranitidine (25 patients) for gastroenterological diseases. Total and HDL cholesterol and total triglycerides have been measured. Ranitidine did not influence the investigated parameters, while cimetidine produced a significant increase in the HDL cholesterol serum concentration ($P = 0.008$).

Keywords cimetidine ranitidine HDL cholesterol

Introduction

Plasma high density lipoprotein (HDL) concentrations are important in the evaluation of atherosclerotic risk (Gordon *et al.*, 1977; Miller & Miller, 1975). Cimetidine-induced increase of HDL-cholesterol has been recently reported in normolipidaemic subjects (Bolton *et al.*, 1983) and in one patient with familial type III^o hyperlipoproteinemia (Miller & Lewis, 1983).

These findings and the different effects of cimetidine and ranitidine on hepatic drug metabolism (Henry *et al.*, 1980; Puurunen & Pelkonen, 1979; Somogyi & Gugler, 1982) and on androgen activity (Funder *et al.*, 1979; Pearce *et al.*, 1980; Winters *et al.*, 1979) stimulated us to investigate the action of these two drugs on plasma lipid patterns in patients suffering from gastroenterological disease.

Methods

Fifty-six patients (44 males and 12 females; mean age 54 years) entered the study and were randomly allocated to cimetidine (400 mg twice daily) or ranitidine (150 mg twice daily) treatment for 5 weeks. Endoscopic diagnoses were

duodenal ulcers (38), gastric ulcers (11) and reflux oesophagitis (7).

Uncooperative patients and subjects treated with cimetidine, ranitidine or hypolipidaemic drugs in the previous 2 weeks did not participate.

Before entering the study, patients underwent a full physical examination and parameters reported in Table 1 were recorded. Before and after treatment, serum total cholesterol, HDL, and total triglycerides were determined.

During the treatment period neither alimentary restrictions nor physical activity variations were prescribed. Compliance and dyspepsia were checked every 2 weeks by interviewing the patients.

Total cholesterol was determined by an enzymatic colorimetric method according to Trinder (CliniCal, Farmitalia-Carlo Erba, Milan), HDL-cholesterol by application of the same method on the supernatant after polyethyleneglycol precipitation of LDL and VLDL (Chemetest, Chemetron Chimica, Milan), and triglycerides by an enzymatic u.v. method (Rapid Test, Roche, Basel). All these determinations were adapted to an Eppendorf ACP 5040 spectrophotometer.

Statistical analysis was performed by Chi-square and Student's *t*-test where appropriate.

Results

Twenty-six patients treated with cimetidine and 25 treated with ranitidine completed the study. Three patients on cimetidine and two on ranitidine withdrew for non-medical reasons. Both groups were comparable but the average age of the ranitidine group was slightly greater than that of the cimetidine group ($P = 0.04$) (Table 1).

Neither cimetidine nor ranitidine modified the total cholesterol (before 174.0 ± 33.3 , after 181.4 ± 30.4 mg/100 ml, and before 170.7 ± 41.5 after 175.2 ± 34.0 mg/100 ml respectively) or triglycerides (before 138.9 ± 77.0 after 145.9 ± 62.6 mg/100 ml, and before 120.8 ± 32.7 after 137.4 ± 49.1 mg/100 ml respectively) concentration. Ranitidine did not affect the HDL-cholesterol level (before 39.7 ± 11.7 , after 38.0 ± 13.9 mg/100 ml) while cimetidine increased it significantly (from 36.9 ± 9.3 to 41.9 ± 12.34 mg/100 ml) (Student's *t*-test for paired data within the group: $P = 0.008$) (Figure 1).

Discussion

Our study has demonstrated a significant increase in HDL-cholesterol concentration in patients treated with cimetidine for dyspepsia and studied without reference to the basal lipid profile.

Bolton *et al.* (1983) noted a decrease of anti-pyrene clearance and, simultaneously, an increase of HDL-cholesterol concentration during cimetidine treatment in normolipidaemic subjects.

Miller & Lewis (1983) suggested that these results could be due to the anti-androgenic action of cimetidine (Funder & Mercer, 1979; Winters *et al.*, 1979).

Our results showing different effects of cimetidine and ranitidine on HDL-cholesterol could be associated with differential androgenic effects.

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Table 1 Patients general data. Figures are mean (s.d.) or absolute numbers (%)

	Cimetidine (n = 26)	Ranitidine (n = 25)
Age (years)	50.1 (14.2)	58.1 (13.6)*
Male	20	21
Female	6	4
Weight (kg)	66.5 (8.3)	68.3 (8.9)
Smokers (%)	12 (41.6)	14 (56.0)
Alcohol consumers (%)	10 (38.5)	8 (32.0)
Coffee drinkers (%)	3 (11.5)	4 (16.0)
Days of therapy	37.0 (7.8)	38.2 (9.3)
<i>Endoscopy</i>		
Duodenal ulcer (%)	19 (73.1)	16 (64.0)
Gastric ulcer (%)	5 (19.2)	5 (20.0)
Oesophagitis (%)	2 (7.7)	4 (16.0)
<i>Base-line lipids</i>		
Total cholesterol (mg %)	174.0 (33.3)	170.7 (41.5)
HDL cholesterol (mg %)	36.9 (9.3)	39.7 (11.7)
Triglycerides (mg %)	138.9 (77.0)	120.8 (32.7)

* $P = 0.04$ (Student's *t*-test). All the other differences between groups are not statistically significant.

Figure 1 Individual and mean values of serum HDL-cholesterol concentration before and after treatment with cimetidine (400 mg twice daily for 37 days) and ranitidine (150 mg twice daily for 38 days).

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