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EFFECT OF MANIDIPINE-SIMVASTATIN COMBINATION ON FIBRINOLYSIS, ADHESION MOLECULES AND C-REACTIVE PROTEIN IN HYPERTENSIVE HYPERCHOLESTEROLEMIC PATIENTS

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Aim of this study was to evaluate the effect of manidipine-simvastatin combination on plasma tissue plasminogen activator (t-PA) and inhibitor (PAI-1) activity, on plasma intercellurar adhesion molecule type-1 (ICAM-1) and on serum C-reactive protein (CRP) in hypertensive, hypercholesterolemic patients.

After 4 week placebo run-in period, 36 hypertensive [diastolic blood pressure (DBP) $>$ 90 and $<$ 105 mmHg], hypercholesterolemic [total cholesterol (TC) $>$ 200 mg/dl] patients were randomized to manidipine 20 mg or simvastatin 40 mg or manidipine-simvastatin combination, according to a 3 x 3 cross over design; each treatment had 12 week duration. Thirty patients completed the study.

The last day of the placebo run-in period and of each treatment period blood pressure was measured and a venous blood sample was taken (at the same hour in the morning) to evaluate plasma t-PA and PAI-1 activity, TC, plasma ICAM-1 and CRP.

The main results are shown in the table.

These results suggest that in hypertensive, hyperchoelsterolemic patients manidipine-simvastatin combination improves the fibrinolytic balance, reduces the plasma ICAM-1 and decreases BP more than single monotherapy. The concomitant cholesterol and CRP reduction suggests that manidipine-simvastatin combination could be the treatment of choice in hypertensive hypercholesterolemic patients.

Main Results

	Placebo	Manidipine	Simvastatin	Combination
SBP (mmHg)	159.8 ± 12.1	140.5 ± 10.7**	155.4 ± 11.9*	137.1 ± 9.3****
DBP (mmHg)	100.7 ± 6.2	84.1 ± 4.8**	98.2 ± 6.2	81.9 ± 4.7***
t-PA (U/ml)	0.49 ± 0.13	0.71 ± 0.19*	0.51 ± 0.14	0.73 ± 0.20*
PAI-1 (U/ml)	24.6 ± 12.3	24.9 ± 12.6	16.1 ± 7.3*	15.9 ± 7.1*
TC (mg/dl)	254.9 ± 28.2	253.8 ± 29.6	202.2 ± 26.4*	201.4 ± 26.5**
ICAM-1 (ng/ml)	237.8 ± 35.6	220.2 ± 29.8*	207.4 ± 26*	190.1 ± 24.6**
CRP (mg/dl)	0.39 ± 0.22	0.34 ± 0.20	0.16 ± 0.12*	0.14 ± 0.08*

** $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ vs placebo*

Key Words: Antihypertensive Therapy, Fibrinolysis, Hypercholesterolemia

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STUDY ON HYPERCOAGULATION AND HYPOFIBRINOLYSIS STATE IN PATIENTS WITH ATRIAL FIBRILLATION AND ESSENTIAL HYPERTENSION

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Objective: To study the change of coagulation and fibrinolysis system and its clinical significance in patients with atrial fibrillation and essential hypertension.

Methods: We performed a study in 54 chronic nonvalvular atrial fibrillation (NVAF) patients (AF group, 28 men and 26 women, aged 58.4±12.3 years), 40 sinus rhythm patients with the same cardiovascular history as NVAF patients (SR group, 20 men and 20 women, aged 57.6±11.7 years), and 35 matched healthy control subjects in sinus rhythm (C group, 17 men and 18 women, aged 52.4±18.5 years). Plasma levels of fibrinogen (FIB), fibrin d-dimer (D-D), tissue plasminogen activator (tPA), its inhibitor (PAI), prothrombin time (PT) , thrombin time (TT) and activated part thromboplastin time (APTT) were measured in plasma from each groups above.

Results: Patients with chronic NVAF had higher plasma FIB, D-D and PAI levels as compared with SR group and C group, While tPA was lower in AF group than the others. There was no significant differences in PT, TT and APTT in the three groups.

Conclusion: There is a hypercoagulation and hypofibrinolysis state in chronic nonvalvular atrial fibrillation patients.

Key Words: Atrial Fibrillation, Coagulation, Hypertension

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HAEMORHEOLOGIC ALTERATIONS IN WHITE COAT HYPERTENSION

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Introduction: The 24 hours monitoring blood pressure has allowed the discrimination between hypertension and white coat hypertension. Several works have shown haemorheolgic alterations in hipertensive patients that might be related with the increased risk for cardiovascular events. The objective of the present work was to evaluate if any alteration in haemorheologic parameters was present in the WCH.

Material and Methods: A non-smokers population of 151 individuals, otherwise healthy, except for hypertension, was studied, and divided in normotensives (NT), white coat hypertensives (WCH), and sustained hypertension (HT). All hypertensive patients were under medication. Blood pressure was evaluated using one device Space Lab 90027. WCH defined as office arterial systolic pressure $\geq$ 140 mmHg and diastolic pressure $\geq$ 90, and ambulatory daytime pressures $<$ 130/80 mmHg. It was determined erythrocyte aggregation, fibrinogen, erythrocyte filtration and plasma viscosity.

It was used the ANOVA statistical model, with the Scheffé's multiple comparison test. It was considered statistically significant values of $p<0,01$ (two-tailed).

Results: There is increasing fibrinogen and plasma viscosity between normotensives and white coat hypertensives, and between those and hypertensives.

Conclusions: The increased fibrinogen and plasma viscosity in WCH suggest that this condition might be also looked as a marker for increased cardiovascular risk.

	N (51)	WCH (50)	HT (50)	P
Age	44.4±11.5	47.3±10.5	45.3±11.0	n.s.
Sex (M/F)	41/10	42/8	42/8	n.s.
BMI	26.1±1.2	26.2±1.6	26.3±1.7	n.s.
SBP casual	118.2±8.2	142.3±8.8	153.7±10.3	<0.01
DBP casual	70.3±5.8	92.3±6.9	91.5±8.3	<0.01
ABPM-SBP	110.2±7.2	111.2±8.4	140.1±11.2	<0.01
ABPM-DBP	68.3±8.4	69.2±9.1	88.9±9.2	<0.01
Haemoglobin	15.1±1.3	14.9±1.5	14.8±1.6	n.s.
Haematocrit	46.4±2.1	46.2±2.2	45.2±2.1	n.s.
ESR	5.3±4.2	10.3±5.6	15.1±12.1	n.s.
Fibrinogen	223.8±94.5	314.3±97.4	389.1±110.0	<0.01
Plasma viscosity	1.12±0.07	1.220±0.13	1.36±0.14	<0.01

Key Words: Fibrinogen, Hypertension, White Coat Hypertension

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