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ATORVASTATIN-AMLODIPINE COMBINATION AND FIBRINOLYTIC BALANCE IN HYPERTENSIVE HYPERCHOLESTEROLEMIC INSULIN-RESISTENT PATIENTS

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Aim of this study was to evaluate the effect of amlodipine-atorvastatin combination on plasma tissue plasminogen activator (t-PA) and inhibitor (PAI-1) activity in hypertensive, hypercholesterolemic patients with insulin resistance which are characterized by impaired fibrinolysis.

After 4 week placebo run-in period, 56 hypertensive [diastolic blood pressure (DBP) $\geq$ 95 and $\leq$ 105 mmHg], hypercholesterolemic [total cholesterol (TC) $>$ 200 mg/dl)], and insulin-resistent [homeostasis model assessment (HOMA index) $>$ 2.5] patients were randomized to amlodipine 5 mg or atorvastatin 20 mg or amlodipine-atorvastatin combination, according to a 3 $\times$ 3 cross over design; each treatment had 12 week duration. Forty-one 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, and fasting plasma glucose (FPG).

The main results are shown in the table.These results suggest that in hypertensive, hyperchoelsterolemic patients with impaired insulin sensitivity amlodipine-atorvastatin combination improves the fibrinolytic balance and decreases BP more than single monotherapy. The concomitant hypocholesterolemic effect suggests that amlodipine-atorvastatin combination could be the treatment of choice in hypertensive hypercholesterolemic patients with impaired fibrinolysis.

Main Results±

	Placebo	Amlodipine	Atorvastatin	Combination
SBP (mmHg)	160.1 ± 12	144.9 ± 11.8**	157.8 ± 12	140.3 ± 11.1***
DBP (mmHg)	99.5 ± 5.3	86.5 ± 5.1**	97.1 ± 5.2	83.2 ± 4.9***
t-PA (U/ml)	0.49 ± 0.12	0.77 ± 0.17*	0.54 ± 0.13	0.81 ± 0.19*
PAI-1 (U/ml)	23.9 ± 11	23.7 ± 11	15.2 ± 7*	14.8 ± 6.9*
TC (mg/dl)	252.5 ± 26	249.5 ± 26	202 ± 28**	199 ± 27**
FPG (mg/dl)	101 ± 8	100 ± 7	101 ± 6	99 ± 8

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

Key Words: Hypertension, Insuline Resistence, Hypercholesterolemia

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EFFECT OF MANIDIPINE AND ATENOLOL ON PLATELET AGGREGABILITY IN ISOLATED SYSTOLIC HYPERTENSION WITH AND WITHOUT TYPE 2 DIABETES MELLITUS

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Aim : of this study was to compare the effect of treatment with manidipine or atenolol on thrombin-mediated platelet aggregation in elderly patients with isolated systolic hypertension and type 2 diabetes mellitus.

Methods: After 4 wash-out run-in period 60 elderly patients (aged 65–80 years) with isolated systolic hypertension (SBP $>$ 140 mmHg and DBP $<$ 90 mmHg) were enrolled : 30 of them had a concomitant well controlled type 2 diabetes mellitus (HbA1c $<=$ 6.5%), the other 30 were the control group. All the patients were randomized to manidipine 10 mg or atenolol 50 mg according to a cross over design; each treatment had a 6 week duration.The last day of the wash-out run-in period and of each treatment period blood pressure was measured and a venous sample was drawn in the morning at the same hour to evaluate platelet aggregation (PA).

Results: The 2 drugs induced a significant and similar blood pressure reduction both in diabetic and non diabetic hypertensives, but manidipine improved platelet aggregation while atenolol did not effect it. The main results are shown in the table. In non diabetic patients manidipine inhibited platelet aggregation only when induced by the higher doses of both ADP and collagen.

Conclusion: these data suggest that the anti-aggregatory effect of manidipine could be of clinical benefit in preventing cardiovascular complications in elderly patients with isolated systolic hypertension and concomitant type 2 diabetes.

Main Results

	PA by ADP 1.6μmol	PA by ADP 10μmol	PA by Collagen 0.25μg	PA by Collagen 0.50μg
Diabetic hypertensive				
Placebo	47.9 ± 13	95.6 ± 11	46.2 ± 14	85.7 ± 10
Manidipine	26.5 ± 12*	60.3 ± 10**	23.1 ± 8**	59.9 ± 7***
Atenolol	45.2 ± 14	90.3 ± 12	41.9 ± 13	79.4 ± 10
Non diabet hypertensive				
Placebo	26.8 ± 8°	70.2 ± 10°	33.9 ± 15	62.6 ± 12°
Manidipine	17.6 ± 7	54.4 ± 8*	24.1 ± 13	49.7 ± 8*
Atenolol	27.9 ± 8	69.3 ± 11	32.7 ± 15	60.4 ± 13

** $p < 0,05$ ** $p < 0.01$ *** $p < 0.001$ vs placebo ° $p < 0.05$ vs diabetic patients*

Key Words: Isolated Systolic Hypertension, Diabetes, Platelet Aggregability

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LOSARTAN ON FIBRINOLYTIC SYSTEM IN HYPERTENSION

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Fibrinolytic system is reported to be altered in patients with hypertension; controversies on action induced by antihypertensive drugs have arisen. The aim of this study was to evaluate action of losartan on fibrinolytic system.

Thirty untreated hypertensive patients (age: 51.34 ± 1.54 years, 15 males 15 females) was studied. Determination of fibrinogen, plasminogen, tissue type plasminogen activator (t-PA), and plasminogen activator inhibitor-1 (PAI-1) were performed at baseline and at the end of six week treatment with losartan. All measurement carried out between 7am and 9am. Initial 50 mg losartan dosage was adjusted to 100 mg once daily if DBP, in sitting position, at week 2 was not below 90 mmHg.

A summary of results are shown as follows:

	Baseline**	After Losartan**	P value***
SBP (mmHg)*	169.7 +/− 4.1	146 +/− 2.7	0.001
DBP (mmHg)*	105 +/− 1.8	91 +/− 1.9	0.001
MAP (mmHg)*	126.6 +/− 2.4	109.9 +/− 2.0	0.001
Fibrinogen (mg/dl)	309.5 +/− 11.9	286.8 +/− 11.34	0.014
Plasminogen (%)	86.3 +/− 2.64	89.84 +/− 2.4	0.233
t-PA (ng/ml)	7.508 +/− 0.43	6.22 +/− 0.39	0.031
PAI-1 (ng/ml)	58.69 +/− 2.91	52.1 +/− 3.53	0.020

** Office Blood Pressure, Sitting Position. ** mean +/− Standard Error. *** Paired Student T test*

In conclusion, losartan in a dosage of 50 to 100 mg/daily reduced significantly blood pressure, fibrinogen, t-PA and PAI-1. Results indicate losartan might reduce thrombotic risk factors in patients with hypertension.

Key Words: Fibrinolytic System, Losartan,