P-92

HIGH PULSE PRESSURE BUT NOT MEAN ARTERIAL BLOOD PRESSURE IS ASSOCIATED WITH ABNORMAL THROMBOGENESIS AND ENDOTHELIAL DAMAGE/DYSFUNCTION IN PATIENTS WITH CORONARY HEART DISEASE WITH AND WITHOUT HYPERTENSION

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Both pulse pressure (PP) and mean arterial blood pressure (MAP) have been implicated as independent predictors of cardiovascular (CV) risk. PP measures the 'pulsatile component', whereas MAP measures the 'steady component' of BP. We hypothesized that high 24-hour ambulatory PP in patients with coronary heart disease (CHD) is associated with an increased risk of hemostasis, which may be related to abnormal hemorheology (raised hematocrit, plasma viscosity and fibrinogen levels), endothelial damage/dysfunction (raised plasma von Willebrand factor, vWf), thrombogenesis (raised D-dimer, Dd) and platelet activation (raised soluble P-selectin, sPsel).

We studied 72 patients with stable CHD who were in sinus rhythm and with preserved left ventricular systolic function (mean ejection fraction 61±10%). All completed a 24-hour ambulatory BP monitoring. Patients were divided into 2 groups according to high (above median) or low (below median) values of the ambulatory PP (51 mmHg). 24-hour PP was positively correlated with age (r=0.48), vWf (r=0.41), Dd (r=0.25), fibrinogen (r=0.3) and sPsel (r=0.22) levels (all $p<0.05$). None of hemostatic indices correlated with 24-hour MAP. On multivariate ANCOVA analysis, after controlling for age, vWf, fibrinogen, Dd and sPsel levels remained significantly elevated in patients with high 24-hour PP (all $p<0.05$).

	High PP (n = 37)	Low PP (n = 35)	P-value
Age (year)	63 ± 11	55 ± 9	<0.001*
Male (%)	31 (84)	28 (80)	0.67
History of hypertension	14 (38)	15 (43)	0.66
Smoker (%)	12 (32)	10 (29)	0.72
Diabetes (%)	9 (24)	6 (17)	0.45
BMI (kg/m^2)	28 ± 3.8	27 ± 3.6	0.38
vWf (iu/dl)	212 ± 58	172 ± 49	0.002*
D-dimer (mg/l)	0.35 (0.23–0.59)	0.24 (0.21–0.35)	0.004*
Fibrinogen (g/l)	3.4 ± 0.8	3.0 ± 0.8	0.025*
Soluble P-selectin (ng/ml)	87 (77–98)	78 (63–91)	0.034*
Plasma viscosity (mpa.s)	1.72 ± 0.2	1.69 ± 0.1	0.31
Hematocrit (%)	39.2 ± 3.6	40.3 ± 3.6	0.12

Mean ± sd or median (IQR). PP, Pulse pressure; vWf, von Willebrand factor; BMI, Body mass index.

High 24-hour PP load in patients with CHD was associated with a prothrombotic state (with higher levels of fibrinogen, Dd and sPsel) and evidence of endothelial damage/dysfunction (vWf), independently of age. These may contribute to higher CV risk associated with increased PP.

Key Words: Pulse Pressure, Thrombogenesis, Endothelial Dysfunction

P-93

POSITIVE EFFECT OF A LOW DOSE COMBINATION OF PERINDOPRIL/ INDAPAMIDE ON THE D-DIMERS AND THE ENDOTHELIAL FACTORS IN HYPERTENSIVE PATIENTS

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Objective: The objective is to evaluate the beneficial effect of treatment based on the low dose combination Perindopril 2mg/Indapamide 0.625mg (Per/Ind) vs. atenolol (Ate) on change in D–Dimers and endothelial factors in hypertensive patients after 6 months of treatment.

Methods: The design was a 6-month, randomised, double blind, 2 parallel group (Per/Ind and Ate) study after a 2 to 4 week run in period. It was possible to adapt treatment to Per 4 mg/Ind 1.25 mg or ate 100 mg according to the blood pressure. Thirty-nine hypertensive patients (90≤DBP<115 mmHg and 140≤SBP<210mmHg - male 71.8%; age 56.2±12.8) with data at baseline and under treatment were analysed by intention to treat.

Results: The results demonstrated significant decreases of D–Dimers, sI-CAM, sE-selectin in the Per/Ind group and a borderline significant reduction of the von Willebrand factor (vWF). Patients on atenolol showed a significant decrease of the sE selectin and vWF. Safety was good in the 2 groups with no unexpected adverse events.

Factors/BP	Per/Ind (n = 18)	Ate (n = 21)
D-dimers (μg/mL)[1] median[Q1 ; Q3]	−1.4** [−2.5; −0.5]	0.5 [−1.6; 1.5]
vWF (IU/dL) median[Q1 ; Q3]	−9.5§ [−17.0; 4.0]	−5.0* [−23.0; 3.0]
sI-CAM (ng/mL)[2] mean ± SD	−14.6 ± 24.8*	3.5 ± 24.5ns
sE-selectin(ng/mL)[2] mean ± SD	−5.2 ± 5.5**	−5.4 ± 5.6***
SBP (mmHg)- mean ± SD	−13.6 ± 20.3**	−11.5 ± 22.3*
DBP (mmHg)- mean ± SD	−7.8 ± 9.4**	−10.0 ± 10.1***

** p < 0.05 ** p < 0.01 *** p < 0.001 § p = 0.06 Student t test or Wilcoxon test for D-Dimers and vwf. [1](ate n = 20); [2](ate n = 18).*

Conclusion: The low dose combination Perindopril 2 mg/Indapamide 0.625 mg, and to a lesser degree atenolol, have induced significant decreases of D–Dimers and endothelial factors affecting the coagulation process. These positive effects may protect from thrombogenesis and add to the benefit of hypertensive treatments on cardiovascular morbidity

Key Words: Thrombogenesis, Endothelial Factors, Perindopril