M14 DO CARDIOVASCULAR AND CEREBROVASCULAR RISK SCORES BASED ON THE FRAMINGHAM EQUATION CORRELATE WITH VON WILLEBRAND FACTOR, A MARKER FOR ENDOTHELIAL DAMAGE AND VASCULAR ENDOTHELIAL GROWTH FACTOR, A MARKER FOR ANGIOGENESIS?

DC FELMEN, CGC SPENCER, F BELGORE, AD BLANN, DG BEEVERS, GYH LIP

University Department of Medicine, City Hospital, Birmingham B18 7QH

Background: Hypertensive patients are at particular high risk of thrombotic and atherothrombotic complications. Endothelial damage and abnormal angiogenesis play an important role in precipitating these thrombotic events.

Methods: We analyzed plasma levels of von Willebrand Factor (vWF) and Vascular Endothelial Growth Factor (VEGF) using ELISA methods in 177 consecutive hypertensives (130 male, mean age 62 (SD) years) and 21 controls (11 male, mean age 58 (SD) years). The subjects were assessed for cardiovascular risk factors including age, sex, smoking habit, blood pressure, serum cholesterol, left ventricular hypertrophy on ECG, and diabetes mellitus. Using the Framingham risk calculator a coronary heart disease (CHD) and stroke risk score were derived. Risk scores from the combined group were correlated (Spearman's method) with plasma levels of vWF and VEGF.

Results: vWF [IU/ml] 0.209 <0.01 0.280 <0.05 VEGF [pg/ml] 0.263 <0.01 0.286 <0.01

Results are presented as correlation coefficient (R) and p-value. Apart from a borderline significant correlation between VEGF and total cholesterol (R=0.189, p=0.046), there was no significant correlation between vWF or VEGF and the individual risk factors.

Conclusion: Vascular endothelial growth factor and endothelial damage as assessed by vWF are correlated with the cerebrovascular and coronary heart disease risk according to the Framingham equation. These markers of endothelial damage and angiogenesis might assist in evaluating the cardiovascular and cerebrovascular risk profile of hypertensive patients.

M15 RELATIONSHIP BETWEEN ENDOTHELIAL DAMAGE, ANGIOGENESIS AND CARDIOVASCULAR RISK FACTORS IN HEALTHY CONTROLS AND HYPERTENSIVE PATIENTS

DC FELMEN, AD BLANN, CGC SPENCER, DG BEEVERS, F BELGORE, AND GYH LIP

University Department of Medicine, City Hospital, Birmingham B18 7QH

Background: Hypertensive patients are at high risk of vascular complication, which can be related to endothelial damage and/or abnormal angiogenesis as assessed by von Willebrand Factor (vWF) and Endothelial Growth Factor (VEGF) respectively. Methods: We studied 138 consecutive hypertensive patients (103 males, mean age 60 (SD) years) who were assessed for their coronary heart disease (CHD) and cerebrovascular (CVA) risk according to the Framingham equation. Hypertensive patients were divided into a "high-risk" group with ≥3 risk factors and a "low-risk" group with <3 risk factors. Risk factors included: age=55 years, male, smoking cholesterol >6.5 mmol/L, diabetes mellitus, family history of CHD, previous stroke, peripheral vascular disease, LVH on ECG, and Q waves or T wave inversion on ECG. Baseline VEGF and vWF plasma levels of the hypertensive patients were analysed by ELISA and compared with healthy normotensive controls.

Results: Controls Low-risk Hypertensives High-risk Hypertensives p-value Low-risk

N 21 19 119
Age [years] 58 (5.4) 57 (6.6) 60 (6.4) 0.036
CHD risk 11.9 (6.8) 13.1 (6.4) 25.0 (10.9) <0.001
CVA risk 2.3 (1.8) 4.8 (3.2) 20.5 (8.6) <0.001
SBP [mmHg] 132 (17) 135 (19) 162 (16) N.S.
DBP [mmHg] 86 (10) 89 (12) 91 (17) N.S.
VEGF [pg/ml] 50 (10) 160 (120-350) 200 (140-410) 0.001
vWF [IU/ml] 96 (19) 119 (27) 135 (80) 0.02

SH: systolic blood pressure, DBP: diastolic blood pressure; p<0.02 controls vs. low-risk hypertensives, p<0.01 controls vs. high-risk hypertensives. Values are expressed as mean and SD, except VEGF as median and IQR. Statistical analysis for comparison low vs. high risk: unpaired T-Test and Mann-Whitney as appropriate. VEGF or vWF were not significantly correlated with risk factors, apart from weak correlation between VEGF and total cholesterol (Spearman Correlation R=0.189, p=0.046).

Conclusion: High-risk hypertensive patients demonstrate abnormal endothelial damage (vWF) but not angiogenesis (VEGF), although both indices are abnormal compared with normotensive controls. These processes appear to be independent of each other, but might individually contribute to the pathogenesis of cardiovascular risk in hypertension.

M16 THE CHANGE IN ENDOTHELIAL DAMAGE AND VASCULAR ENDOTHELIAL GROWTH FACTOR AS AN INDEX OF ANGIOGENESIS, FOLLOWING INTENSIFIED BLOOD PRESSURE TREATMENT IN HIGH-RISK HYPERTENSIVES

DC FELMEN, CGC SPENCER, F BELGORE, AD BLANN, DG BEEVERS, AND GYH LIP

University Department of Medicine, City Hospital, Birmingham B18 7QH

Background: High-risk hypertensive patients are at particular risk of vascular complications, which may be related to endothelial damage or abnormal angiogenesis as assessed by measurements of von Willebrand Factor (vWF) and Vascular Endothelial Growth Factor (VEGF) respectively. Methods: We studied 136 "high-risk" hypertensive patients (untreated BP≥160/100 mmHg or treated BP≥140/90 mmHg). "High-risk" was defined as ≥3 or more of the following risk factors: age≥55 years, male, smoking, cholesterol >6.5 mmol/L, diabetes mellitus, family history of coronary artery disease, previous ischaemic stroke, peripheral vascular disease, left ventricular hypertrophy on ECG and Q waves or T wave inversion on ECG. Patients were randomly assigned to treatment with amiodipine ± perindopril or atenolol ± bendroflumethiazide-potassium. Endothelial damage and angiogenesis were assessed by measuring vWF and VEGF by ELISA at baseline and after 6 months treatment. Baseline levels were compared with 21 healthy normotensive controls.

Results: Controls High-risk hypertensives at baseline High-risk hypertensives after 6 months treatment

<table>
<thead>
<tr>
<th>N</th>
<th>21</th>
<th>126</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [years]</td>
<td>58 (5.4)</td>
<td>60 (6.6)</td>
</tr>
<tr>
<td>Systolic BP [mmHg]</td>
<td>132 (17)</td>
<td>161 (17.1)</td>
</tr>
<tr>
<td>Diastolic BP [mmHg]</td>
<td>86 (9.7)</td>
<td>91 (10.0)</td>
</tr>
<tr>
<td>VEGF [pg/ml]</td>
<td>50 (18-117)</td>
<td>200 (140-410)</td>
</tr>
<tr>
<td>vWF [IU/ml]</td>
<td>95 (38)</td>
<td>134 (38)</td>
</tr>
</tbody>
</table>

Values are expressed as mean and SD, except VEGF as median and IQR. Statistical analysis: paired and unpaired T-Test as appropriate, except for VEGF. Mann-Whitney Test or paired Wilcoxon Test. I p<0.05 controls vs. Baseline, 2) p<0.05 baseline vs. 6months treatment.

Conclusion: When compared to controls, high-risk hypertensives demonstrate abnormal angiogenesis and endothelial damage, both of which are beneficially reduced following 6 months of antihypertensive treatment. These findings may be pathophysiologically relevant to hypertension and its complications and the beneficial effects of blood pressure lowering.

M17 OXIDATIVE STRESS AND ENDOTHELIAL DAMAGE IN CHRONIC HEART FAILURE: EFFECTS OF CARVEDILOL AND BISOPROLOL

B CHIN, S NUTTALL, M KENDALL, C GIBBS, AD BLANN, GYH LIP

'MRS members

Dir of Med Sciences, University of Birmingham Birmingham UK

Background. There is now convincing evidence for using beta-blockers in the treatment of chronic heart failure (CHF) to control neurohumoral activation. As its use becomes more prevalent, the choice of drugs raises important theoretical and practical questions. Although the second generation compounds carvedilol is beta-selective, the non-selective third generation bisoprolol has ancillary pharmacological properties including anti-oxidant effects Objective. To determine if oxidative stress reduction and endothelial damage/dysfunction is a specific property of carvedilol or related to more general effects of beta adrenergic blockade. Methods. 46 patients with chronic stable heart failure (NYHA II-IV) were randomised to receive carvedilol (start 3.125mg b.d. to max. 25mg b.d.) or bisoprolol (start 1.25mg o.d. to max. 10mg o.d.) in an open-label fashion. All patients were established on an ACE inhibitor and none had creatinine >150mmol/L. Oxidative stress (serum lipid peroxidation (LPO) and total anti-oxidant capacity (TAC)) and von Willebrand factor (vWF) [marker of endothelial damage] were measured at baseline and 2months.