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D-dimer relates positively with increased blood pressure in black South Africans: The SABPA study

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ABSTRACT

Introduction: Hypertension is highly prevalent in black South Africans in which morbidity and mortality from stroke are on the increase. Elevated blood pressure and haemostatic markers can induce changes in blood rheology and endothelial function which could result in a procoagulant state that increases the risk for cerebrovascular disease. Information about the coagulation and fibrinolytic systems of people from African descent are limited. We therefore, investigated the haemostatic profile and its relationships with blood pressure in black South Africans.

Materials and methods: We measured ambulatory blood pressure and haemostatic markers of 201 black and 208 white school teachers. The haemostatic markers included measurements representing coagulation and fibrinolysis (von Willebrand factor, fibrinogen, plasminogen activator inhibitor-1, fibrin D-dimer and clot lysis time).

Results: Black participants displayed significantly higher blood pressure, von Willebrand factor, fibrinogen, plasminogen activator inhibitor-1 and D-dimer levels and longer clot lysis times ($p \leq 0.001$). Single, partial and multiple regression analyses showed that systolic ($p \leq 0.011$) and diastolic blood pressure ($p = 0.010$) correlated positively with D-dimer in black participants, while systolic ($p \leq 0.001$) and daytime diastolic blood pressure ($p = 0.011$) correlated negatively with clot lysis time in white participants.

Conclusion: The black population had a more prothrombotic profile, with higher levels of coagulation markers and inhibited fibrinolysis, than the white study participants. The positive association between blood pressure and elevated D-dimer in the blacks may contribute to the high prevalence of hypertension and related increased cardiovascular and cerebrovascular risk in this group.

Introduction

Abnormalities in the coagulation and fibrinolytic systems such as hypercoagulation and hypofibrinolysis are associated with cardiovascular [1,2] and cerebrovascular disease [3,4]. Morbidity and mortality from cardiovascular [5] and cerebrovascular [6] diseases are rapidly increasing in the black population of South Africa, a group with a high prevalence of hypertension [7,8], that contributes, at least in part, to the low life expectancy of 52.6 years [9].

Available evidence from European populations suggests that elevated blood pressure is associated with high circulating levels of several coagulatory [10,11] and fibrinolytic markers [12,13], inducing changes in blood constituents, flow and endothelial function [14–16]. These studies did not include people from African descent or distinguish between ethnicities. Information on the haemostatic system markers and their associations with cardiovascular function in black South Africans is limited. Current evidence suggest that black populations may have altered levels of haemostatic proteins [17–19] that could increase their cardiovascular and cerebrovascular risk.

We therefore investigated the blood pressure and haemostatic profiles of black and white South Africans and determined associations between ambulatory blood pressure and components of the haemostatic system in these groups.

Materials and methods

Study population

The Sympathetic activity and Ambulatory Blood Pressure in Africans (SABPA) study was a cross-sectional study involving school teachers

Abbreviations: vWF_{ag}, von Willebrand factor antigen; $PAI\text{-}1_{ag}$, Plasminogen activator inhibitor-1 antigen; $PAI\text{-}1_{act}$, Plasminogen activator inhibitor-1 activity; t-PA, tissue Plasminogen activator; CLT, Clot lysis time; ABPM, Ambulatory blood pressure monitor; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; PP, Pulse pressure; BMI, Body mass index; TC, Total cholesterol; LDL, Low density lipoprotein cholesterol; HDL, High density lipoprotein cholesterol; TC:HDL, Total cholesterol: high density lipoprotein cholesterol; CRP, C-reactive protein; HIV, Human immunodeficiency virus.

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Table 1
Characteristics of the study population.

	Black (n = 200)	White (n = 209)	P
Women, n (%)	99 (49.5)	108 (51.6)	0.66
Age, years	44.4 ± 8.1	45.0 ± 10.9	0.49
Body mass index, kg/m^2	30.1 ± 7.0	27.6 ± 5.9	<0.001
Waist circumference, cm (men)	93.6 ± 15.5	101.5 ± 14.4	<0.001
Waist circumference, cm (women)	93.6 ± 15.6	86.0 ± 13.3	<0.001
Haemostatic markers			
von Willebrand factor, %	92.8 ± 24.7	63.1 ± 15.0	<0.001
Fibrinogen, g/L	3.53 ± 0.89	3.07 ± 0.55	<0.001
Plasminogen activator inhibitor-1, ng/ml	35.4 ± 9.7	21.7 ± 6.7	<0.001
Fibrin D-dimer, μg/L	294 (80 – 1180)	209 (68 – 617)	<0.001
Clot lysis time, min	84.6 ± 18.8	75.3 ± 10.7	<0.001
Biochemical measurements			
Total cholesterol, mmol/L	4.60 ± 1.19	5.54 ± 1.28	<0.001
Total cholesterol: high density cholesterol	4.48 ± 2.05	4.99 ± 1.62	<0.001
High density lipoprotein cholesterol, mmol/L	1.12 ± 0.35	1.20 ± 0.41	0.039
Low density lipoprotein cholesterol, mmol/L	2.83 ± 0.98	3.80 ± 1.09	<0.001
Triglycerides, mmol/L	1.43 ± 1.27	1.20 ± 0.76	0.022
Glycosylated hemoglobin A1c, %	5.87 (5.10 — 7.40)	5.47 (5.00 — 6.10)	<0.001
Glucose, mmol/L	5.26 (4.04 — 7.06)	5.61 (4.70 — 6.81)	<0.001
C-reactive protein, mg/L	4.29 (1.76 – 31.05)	2.03 (1.01 – 8.99)	<0.001
Cardiovascular measurements			
24 hour Systolic blood pressure, mmHg	132.6 ± 15.2	123.7 ± 11.2	<0.001
24 hour Diastolic blood pressure, mmHg	83.1 ± 10.1	76.4 ± 7.5	<0.001
24 hour Pulse pressure, mmHg	49.5 ± 8.6	47.2 ± 6.9	0.004
Daytime systolic blood pressure, mmHg	138.1 ±15.0	129.1 ±11.2	<0.001
Daytime diastolic blood pressure, mmHg	88.8 ± 10.2	81.5 ± 8.5	<0.001
Nighttime systolic blood pressure, mmHg	123.2 ± 15.9	113.0 ± 12.1	<0.001
Nighttime diastolic blood pressure, mmHg	74.0 ± 11.6	66.3 ± 7.7	<0.001
Lifestyle			
Physical activity, kcal/day	2564 (1614 – 4022)	2884 (1905 – 4365)	<0.001
Gamma glutamyl transferase, U/L	43.6 (20.0 — 154.7)	17.4 (7.0 — 74.0)	<0.001
Current smoking, n (%)	34 (17.0)	29 (13.9)	0.39
HIV infected, n (%)	19 (9.5)	0 (0.0)	<0.001
Intake of medications			
Anti-hypertensive medication, n (%)	43 (21.5)	18 (8.6)	<0.001
Anti-coagulant medication:			
Wafarin/Heparin, n (%)	2 (1.0)	0 (0.0)	0.15
Asprin, n (%)	4 (2.0)	12 (5.7)	0.058

Values are arithmetic mean ± SD, geometric mean (5th to 95th percentile interval), or number of subjects (%).
Normal reference ranges: [23].
von Willebrand factor, %: 75 — 125.
Fibrinogen, g/L: 1.5 – 4.0.
Plasminogen activator inhibitor-1, ng/ml: 4.0 – 43.0.
Fibrin D-dimer, μg/L: 0 – 500.

(n = 409) between the ages of 25 – 60 years from the North West Province, South Africa. Participants consisted of 200 black (101 men and 99 women) and 209 white (101 men and 108 women) participants. Exclusion criteria were: elevated ear temperature, dependence or abuse of psychotropic substances, regular blood donors, or individuals vaccinated in the previous three months. Informed consent was obtained prior to the commencement of measurements. Each participant completed a lifestyle questionnaire, including questions on smoking and alcohol habits as well as chronic medication use. The study complied with all applicable international regulations and the Helsinki declaration for investigation of human participants. The Ethics Review Board of the North-West University (Potchefstroom Campus) approved the study.

Clinical measurements

A 24-hour ambulatory blood pressure (ABPM) and electrocardiogram apparatus (Meditech CE120® Cardiotens, Budapest, Hungary) was attached to the participants at their workplace. The device was programmed to measure blood pressure at 30 minute intervals during the day (08:00 – 22:00) and every hour during the night (22:00 – 06:00). The electrocardiogram recorded measurements every 5 minutes for 20 seconds. The participants continued with their daily activities and were asked to record any abnormalities such as nausea, headache, physical activity and stress on their ambulatory diary cards. Each participant's energy expenditure during the day was calculated with a validated accelerometer device (Actical® accelerometers, Montréal, Québec). Participants reported to the Metabolic Research Unit of the North-West University at 16:30 where they were informed of the procedures of the following day. They received a standardised meal at 18:00, and final snacks and drinks at 20:30, and were requested to go to bed at around 22:00. At 06:00, the ABPM apparatus was removed, and anthropometric measurements and blood sampling performed. The 24-hour blood pressure and electrocardiogram data were downloaded onto a database using the CardioVisions 1.9.0 Personal Edition software (Meditech, Budapest, Hungary).

Anthropometric measurements

All measurements were taken in triplicate with calibrated instruments. Stature was measured to the nearest 0.1 cm with a stadiometer (Invicta Stadiometer, IP 1465, London, UK), body mass to the nearest 0.1 kg (Precision Health Scale, A & D Company, Tokyo, Japan) and waist circumference to the nearest 0.1 cm with a unstretchable flexible 7 mm wide metal tape (Holtain, Crosswell, Wales) [20,21]. Body mass