

Table of Contents

	Page
Declaration	III
Publications and presentations	IV
Abstract	V
Acknowledgements	VII
List of figures	VIII
List of tables	IX
List of abbreviations	X
1.0 Introduction	1
1.1 Cardiovascular disease	1
1.2 Hypertension	2
1.3 Nitric oxide	5
1.3.1 Nitric oxide synthesis	6
1.4 Arginine	7
1.4.1 Metabolism of L-arginine	9
1.5 Amino acids	12
1.6 Summary	13
1.7 Aims	14
2.0 Materials and Methods	16
2.1 Patients and control subjects	16
2.2 Blood pressure measurements	17
2.3 Blood and urine sampling	17
2.4 Sample preparation and laboratory analysis	18
2.5 HPLC/MS	18
2.6 Data analysis	19
3.0 Results	20
3.1 Patient demographics	20
3.2 Arginine and related amino acids	21
3.2.1 Correlations of amino acids with blood pressure and demographic parameters	21

3.2.2 Urinary amino acids	22
3.3 Multivariate analysis	22
4.0 Discussion and conclusions	32
4.1 Methodology	32
4.2 Arginine and blood pressure	33
References	38

Declaration

I, Cameron Aston Naidoo, declare that this dissertation is my own work. It is being submitted for the degree of Master of Science in Surgery and Biochemistry at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination.

I Certify that the study contained in this dissertation have the approval of the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg. HREC protocol number: M050550.

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Publications and Presentations

Naidoo C. A., Cromarty A. D., Snyman T., Sliwa K., Libhaber E., Essop M. R. and Candy G. P.

2009. Relationships between fasting plasma amino acid concentrations and ambulatory blood pressure in a group of African descent in South Africa. *SAHeart*. Vol. 6, pp 142-147

2010 – Hypertension Society of South Africa. Oral presentation

Surgical Research Society of South Africa. Oral presentation

Bert Myburgh Research Forum, Oral Presentation.

2009 - Bert Myburgh Forum. Oral presentation (3rd Prize)

South African Heart Association. Oral Presentation

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Surgical Research Forum. Oral presentation

2008 - South African Heart Association. Poster presentation

Bert Myburgh Forum. Oral presentation

Interfaculty Research Day. Poster presentation

ABSTRACT

Background: Hypertension is an important modifiable risk factor for cardiovascular disease, the leading cause of mortality and morbidity globally. Blood pressure can be reduced by vasodilators, such as drugs and the semi-essential amino acid arginine, the precursor of the potent vasodilator nitric oxide. Although arginine supplementation has been used to reduce blood pressure, plasma arginine concentrations have been shown to be increased in hypertension. This study measured the concentrations of urinary and plasma amino acids and described associations between arginine related amino acids and their associations with 24 hour ambulatory blood pressure concentrations in Black South African control subjects and patients with hypertension.

Methods: Ninety-seven participants were recruited at the clinics, hospitals and laboratories in Johannesburg area. Twenty four hour ambulatory blood pressure readings were obtained and early morning fasting blood and urine sample were taken with a medical history. Amino acids concentrations were determined using high performance liquid chromatography and mass spectrometry.

Results: Plasma and urinary amino acid concentrations were unchanged in patients with elevated blood pressure compared with normotension. Arginine concentrations correlated positively with amino acids using the same transporter, other urea cycle amino acids, the inhibitor asymmetric dimethylarginine, and strongly with its precursor proline ($r^2 > 0.9$; $p < 0.0001$) even after correcting for amino acid nitrogen ($r^2 > 0.7$; $p < 0.0001$). Elevated urinary arginine concentrations were found to be an independent determinant of both daytime systolic and diastolic blood pressures, with citrulline excretion determining both 24 hour and daytime diastolic pressures. Lysine also correlated with blood pressure and was found to be an independent predictor of blood pressure in multivariate analysis.

Discussion and Conclusions: Lysine shows a novel association with blood pressure. Novel associations should be further investigated as risk factors for cardiovascular disease.

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List of Figures

Figure	Page
1. Arginine Metabolism and Pathways.	11

List of Tables

Table	Page
1.1 – Modifiable and non-modifiable risk factors for cardiovascular disease	4
1.2 – Essential and non-essential amino acids obtained from the hydrolysis Of protein	15
3.1 – Subject demographic data.	25
3.2 – Subject plasma arginine and related amino acid concentrations.	26
3.3 – Associations (Pearson correlation coefficient: r^2) of plasma arginine, blood pressure and other amino acids	27
3.4 – Associations (Pearson correlation coefficient: r^2) of plasma lysine, blood pressure and other amino acids.	28
3.5 – Subject urinary arginine and related amino acid concentrations.	29
3.6 – Multiple regression analysis of determinants of blood pressure.	30
3.7 – Multiple regression analysis of determinants of blood pressure.	31

List of Abbreviations

ABP – Ambulatory blood pressure

ABPM – Ambulatory blood pressure monitor

ADMA – Asymmetric dimethylarginine

BMI – Body mass index

DBP – Diastolic blood pressure

HPLC – High performance liquid chromatography

MS – Mass spectrometry

NO – Nitric oxide

SBP – Systolic blood pressure

tHcys – Total Homocysteine