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EFFECT OF PERINDOPRIL/INDAPAMIDE VERSUS ATENOLOL ON ANGIOGENESIS AND ENDOTHELIAL FUNCTION IN ESSENTIAL HYPERTENSION

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We compared the effect of perindopril/indapamide combination compared to atenolol on endothelial function and angiogenesis in essential hypertension over 6 months.

34 patients (25 male, mean age 57.7±SD12.6years) with systolic blood pressure (SBP) ≥160mmHg and diastolic blood pressure (DBP) ≥90mmHg were randomised (double blind) to fixed low dose perindopril2mg/indapamide0.625mg combination or atenolol 50 mg once a day. Treatment doses were doubled at 12 weeks if SBP ≥160mmHg or DBP≥95mmHg. Plasma samples were taken at weeks 0, 12 and 24. They were analysed by ELISA for levels of vascular endothelial growth factor (VEGF), a marker of angiogenesis, and levels of von Willebrand factor (vWf), E-selectin (E-sel) and soluble thrombomodulin (sTM), markers of endothelial function.

Baseline demographics, blood pressure and plasma levels of VEGF, vWf, E-sel and STM in the 2 groups were similar. SBP and DBP changes were comparable (see table); inter-group analysis showed similar SBP (p=0.94) and DBP (p=0.52) reductions. There were significant reductions in plasma VEGF in both groups (see table). There were no significant changes in any indices of endothelial function in either group.

We have shown reductions in levels of angiogenesis (VEGF) with the treatment of hypertension, with no significant changes in endothelial function (vWf, sTM, E-sel). This would suggest that changes in angiogenesis can occur independently of endothelial function in essential hypertension and is not reliant on the mechanism of blood pressure reduction.

Changes in Levels of Blood Pressure and Plasma Indices in Perindopril/Indapamide versus Atenolol Treatment Groups over Six Months

	Perindopril/Indapamide Treatment Group			Atenolol Treatment Group		
	Week 0	Week 12	Week 24	Week 0	Week 12	Week 24
SBP (mmHg)	164 ± 18	148 ± 17	150 ± 19	161 ± 15	145 ± 15	148 ± 21†
DBP (mmHg)	99 ± 5	90 ± 8	90 ± 11	100 ± 7	90 ± 11	89 ± 9†
VEGF (pg/ml)	5150[988–9625]	650[80–3200]	115[50–525]	3400[2000–6000]	440[103–2375]	95[49–770]*
vWf (IU/dl)	131 ± 40	132 ± 17	118 ± 25	126 ± 31	122 ± 29	116 ± 24
sTM (ng/ml)	49.7 ± 18.6	55.3 ± 17.1	54.7 ± 22.5	47.1 ± 14.9	44.4 ± 16.6	47.7 ± 15.4
E-sel (ng/ml)	57.2 ± 14.6	52.7 ± 11.7	51.5 ± 10.5	56.5 ± 10.9	55.7 ± 10.6	51.8 ± 9.7

*† $p < 0.05$, * $p < 0.001$. Results expressed as mean ± standard deviation or median [interquartile range]. Results analysed by repeated measures ANOVA or Friedman's test.*

Key Words: Angiogenesis, Endothelial Function,

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THE RED BLOOD CELL (RBC) ARGENINE-NITRIC OXIDE PATHWAY MAY BE RELATED TO THE PHENOPTYPIC EXPRESSION OF LOW RBC POTASSIUM IN HYPERTENSIVES

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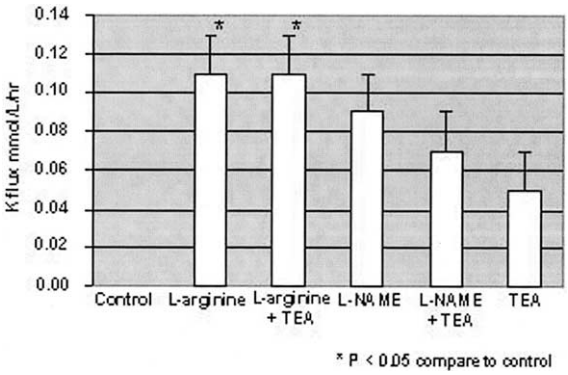
Low RBC K (RBCKi) has been proposed as a potential marker for K changes in other cells involved in blood pressure regulation. Nitric oxide (NO), essential for maintaining vascular tone, is produced from arginine by nitric oxide synthase in several cells including RBC. The aim of this study is to evaluate the effect of the RBC arginine-nitric oxide pathway on K efflux.The present study is part of the NHLBI Family Blood Pressure Program, a large multicenter study of the genetic determinants of high BP. The present analysis includes in vitro experiments using RBC from volunteers. Venous blood samples were obtained in heparinized vacuum tubes and centrifuged immediately (3500 r.p.m. × 10 min), plasma and RBC were separated and buffy coat was discarded. RBC preparations and incubations were carried out within 2-4 hours after blood collection. Incubation: 50μl of RBC were suspended in 5 ml of buffer physiologic solution and incubated at 37°C for 1 hour in presence of various chemical agents: a) NOS inhibitor 10^3 M (L-NAME) with or without a 10^8 M of K channel inhibitor tetraethylammonium chloride (TEA); b) 10^5 M of NO precursor (L-arginine) with or without TEA; c) TEA; d) control. After the incubation period, samples were centrifuged 2000 r.p.m. × 10 min and K was measured in the supernatant by flame photometry. Potassium flux was significantly greater in presence of L-arginine independently of the presence of TEA. K flux was no different from control in presence of L-NAME with or without TEA, and in presence of TEA alone.We conclude that RBC arginine-NO pathway affects K flux through a mechanism other than the intermediate-conductance calcium dependent K channels and that RBC arginine-NO pathway could be involved in the phenotypic expression of low RBCKi in hypertensives.



Key Words: RBC Potassium, Nitric Oxide, Hypertension