Translational Characterization of Blood Pressure Changes Following the DASH Diet– When the Kidneys React to Nutritional Changes

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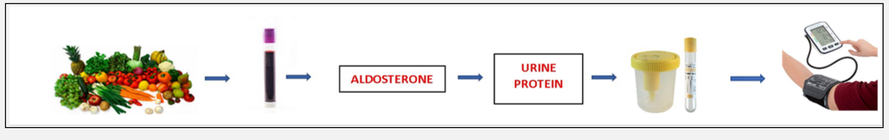
Introduction: Hypertension is a disease of the western world, as it stems from lifestyle habits. Lower salt consumption reduces blood pressure, yet the DASH diet is much more effective, lowering blood pressure as efficiently as one anti-hypertensive drug. The precise mechanism through which DASH achieves its effect is not understood, and this is the project goal.

Aim: We hypothesize that exposing hypertensive volunteers to a high potassium and low sodium DASH diet will change the composition of renal ion channels in an aldosterone-dependent manner, leading to excretion of both sodium and potassium and a reduction in blood pressure. To assess how the nutritional change modifies ion channel composition in the kidneys' epithelium, we will monitor urine exosomes, which contain epithelial cell membranes.

Figure 1 : The causal pathway to characterize the mechanism of the DASH diet, underscored by a list of performance indicators we will measure to test the hypothesis.



Intervention – potassium rich diet

Effect 1 – increased serum potassium

Effect 2 – increased aldosterone

Effect 3 - Change in the abundance of excreted renal tubular proteins

Effect 4 - change in ratio of urine Na/K

Outcome – blood pressure reduction

Table 1. Demographics and vital signs of volunteers who completed the study. 24-hour ABPM (ambulatory blood pressure monitor) were conducted on day 1 and day 10 of the exposure to DASH. This was done in parallel to 24-hour urine collection. We monitored participants' weight, renal function and blood electrolytes to identify and intervene with changes that could interfere with response.

Participant ID	DBI-3	DBI-6	DBI-7	DBI-11	DBI-14
Age	57	45	51	39	34
Gender	M	M	M	F	M
Race	W	B	B	B	B
BMI	23	26.4	29.3	28.4	29.9
DASH Potassium consumption (mg/d)	5594	4903	5920	4899	6007
24-hour mean ABPM 1 (day 1)	130/81	128/83	155/101	120/76	138/83
24-hour mean ABPM 2 (day 10)	124/78	130/89	140/89	112/68	137/80
24-hour urine volume day 1 (ml)	5060	2830	3010	2025	1220
serum creatinine (mg/dl)	1	1.1	1.3	0.7	1.2
urine creatinine (mg/24 hour)	810	1302	3191	911	2208
creatinine clearance 1	83	70	130	79	140
24-H potassium content	23	25	96	61	54
24-H sodium content	65	71	196	97	146
24-H Na/K	2.83	2.84	2.04	1.59	2.70
sample Na/k	2.78	2.78	2.03	1.6	2.73
24- hour urine volume day 10 (ml)	5575	3210	3350	1410	1370
serum creatinine (mg/dl)	1	1	1.3	0.8	1.2
urine creatinine (mg/24 hour)	1450	2343	1407	874	2384
creatinine clearance 2	95	125	97	86	158
24-H potassium content	22	71	90	70	61
24-H sodium content	31	64	80	70	103
24-H Na/K	1.41	0.90	0.89	1	1.69
sample Na/k	1.13	1.1	0.89	1	1.23

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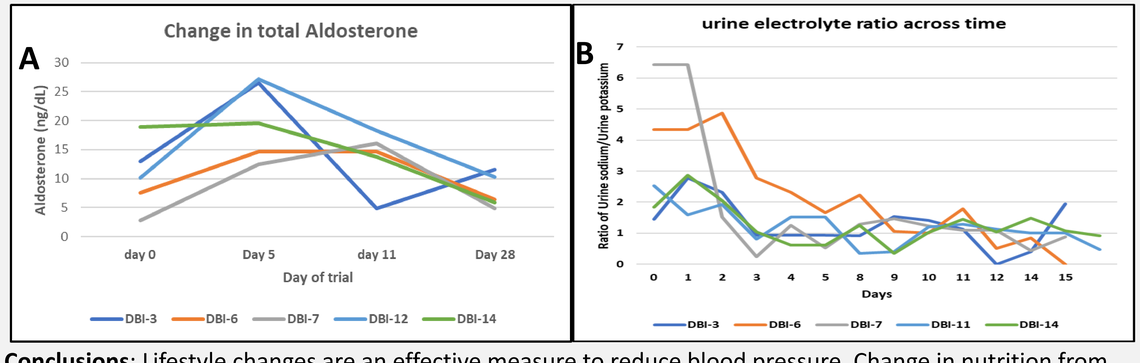
Methods: We designed an in-patient 14-day nutritional study with planned recruitment of 20 volunteers. Participants were screened to exclude use of antihypertensive medication, diabetes, ischemic heart disease, metabolic syndrome, and Renin-Angiotensin axis abnormalities. They completed a detailed nutritional assessment of eating habits prior to admission, and menus were planned to maintain caloric intake and avoid weight reduction. Menus were designed based on the guidelines of the National Heart Blood and Lung Institute (NHBLI) to consume daily low salt (2.3 g of sodium compared to over 4.5 g in a typical American diet) and high potassium (4.7 g). We completed daily measurements of blood pressure, blood and urine electrolytes, aldosterone, and urine for exosomes. Participants completed 2 ambulatory blood pressure measurements (ABPM) on days 1 and 10 of the trial, parallel to collecting 24-hour urine for electrolytes, creatinine and volume. **Results**: Five participants have completed the trial, 80% men, 80% Blacks (table 1). Change in nutrition from American style diet to DASH diet led to high urine output, as expected from the need to dispose of the high potassium. Serum Aldosterone increased following exposure to the high potassium, peaking 5 days after the intervention started, while urine electrolyte ratio (Na/K) reversed from sodium to potassium >2 on day 1 to <1 after 10 days (figure 2). Daily mean blood pressure reductions of 6-15 mmHg were documented by ABPM 10 days after dietary intervention (table 1).

Figure 2: Change in serum Aldosterone (A) and urine electrolytes (B) following nutritional change.



Conclusions: Lifestyle changes are an effective measure to reduce blood pressure. Change in nutrition from western style diet to DASH diet leads to a paradoxical increase in aldosterone, reverse in urine electrolyte ratio and blood pressure reduction in parallel. Urine electrolyte ratio could serve as a monitoring tool to guide patient nutrition. We anticipate urine exosome analysis will reveal a change in ion channel composition and identify a specific protein governing the response.