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Article type : Commentary

Stress-Induced Increase in Blood-Pressure in Young Adult African-Americans: Management by Angiotensin-II Receptor Blocker Therapy?

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Keywords: Mental Stress, Angiotensin-II, Hypertension in African-Americans, Angiotensin-II Receptor Blocker Therapy, Cardiovascular Diseases

Running Head: Stress and Ang-II Receptor Blocker Therapy

Conflict of Interest: The author declares no conflict of interest and that no funds were received for the preparation of this manuscript

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/JCH.13630

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The prevalence of hypertension in African-Americans (AAs) is among the highest in the world and they are at high risk of developing hypertension-related heart, kidney and brain injury [1, 2]. The underlying mechanisms of hypertension in AAs is complex, and combination of genetic and environmental factors play major role. Salt-sensitivity, obesity and diabetes in AAs are well-studied, and are directly correlated with hypertension [3, 4]. There has been an increasing interest on cardiovascular risk factor such as psychological stress in AAs that may contribute to increase in blood-pressure (BP). African-Americans experience high socio-economic disparity even today, and they are 20% more likely to report serious psychological distress than adult whites [5]. Psychological stress may increase the susceptibility and severity of hypertension [6], but it is not clear whether all psychological stress-related BP spikes add-up and result in hypertension in the long-term? Studies are still underway to establish the causality between mental stress and long-term high BP, however, stress is associated with poor diet, smoking, excessive alcohol consumption, anxiety and depression. There is very little information to date on therapeutic interventions of mental stress-induced increase in BP and future cardiovascular events.

In this issue of Journal of Clinical Hypertension [7], Jeong and colleagues from Augusta University presented their findings on the beneficial effects of Angiotensin-II receptor blocker (ARB) irbesartan in attenuating the acute mental stress-induced increase in BP in young adult AAs (25 ± 7 years) [7]. Authors have established the model of acute mental-stressor in AAs, and is associated with mild-increase in systolic/diastolic blood-pressure (SBP/DBP) [8 9]. Stressor is a 45-minute competitive racing or sports video-game played against another individual for a monetary award, followed by 45 minute of recovery

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period. Precise mechanisms of stress-induced increase in BP are not fully understood, and in this report, authors hypothesized activation of renin-angiotensin system (RAS) and Ang-II activity as one potential mechanism. Exclusion criteria of the study included 1) Prescribed BP medication, 2) Pregnant, 3) Food-allergy, 4) Hemoglobin < 14 g/dL, 5) history of angioedema, 6) history of cardiac arrhythmia, 7) serum creatinine >1.6 mg/dL, 8) serum potassium >5.5 mEq/L, or 9) during the menses phase of the menstrual cycle. Screened individuals were pre-tested to ensure no adverse effects of ARB. Overall, this is a well-designed study, placebo-controlled, randomized, double-blind crossover trial with 132 normotensive healthy young adult AAs that were treated either with placebo or ARB (150 mg P.O.) for 1 week before subjecting to 45 minute of stress. This was followed by two-week of washout period and individuals were then subjected to a second stressor test. As this is a crossover study, individuals who were ARB-treated in the 1st stressor test received placebo treatment in the 2nd stressor test, and vice-versa for the placebo group of the 1st stressor test. Hemodynamic parameters during two stress-test (SBP/DBP, heart rate, total peripheral resistance (TPR), stroke volume and cardiac output) were recorded and averaged.

As expected, ARB treated individuals had lower resting BP (SBP/DBP) on the experiment day. Stressor led to a significant increase in BP in placebo group as early as 15 minutes into the mental-stress, while this was delayed in the ARB treated group to 45 min. It is important to note that during stress, increase in BP from the rest was similar in magnitude in both placebo and ARB treated group, the only caveat being, it was delayed in the ARB treated group. It is worth mentioning that, impaired post-stress BP recovery has been associated with unfavorable longitudinal BP changes and increased risk of cardiovascular outcomes [6]. In the recovery period, BP in the ARB treated group dropped below the resting BP, while in placebo group, BP remained elevated and did not return to resting BP even at 45-minute of recovery.

Previously, authors showed significant percentage of young AAs displayed impaired pressure-natriuresis in response to stress [9]. In this study, authors extended their work and demonstrated that ARB improved urinary sodium excretion in young AAs during stress, and this in-part, may explain the attenuated BP response. Furthermore, vasodilatory effect of irbesartan reduced total peripheral resistance in the ARB treated group before, during and after stress test, compared to placebo. Other hemodynamic parameters such as heart rate, stoke volume and cardiac output were not significantly different between ARB and placebo group. The study has several limitations. The small size of the study population warrants further studies in large replication cohorts. Lack of young adult non-AAs control group in this study makes data difficult to interpret in the setting of stress-pressor response. It would be

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interesting to show the percentage of sodium retainer or excreter in non-AAs, compared to AAs. Although, females were 46% of the study size, it is not clear whether authors noticed any sex-based differences. Additionally, the study involves young adult normotensive AAs, thus, therapeutic efficacy and clinical implication of ARBs in hypertensive AAs who experience mental-stress in every day's life remains unclear.

Major finding of the study is that authors identified the potential role of increased Ang-II and RAS activity in the stress-induced hemodynamic regulation in young adult healthy AAs, and ARB treatment delayed increase in BP, improved natriuresis and reduced TPR. Authors provided some evidence of blocking Ang-II activity by irbesartan in improving hemodynamic response in young AAs. Beneficial effects of ARB were associated at least in part, by vasodilation and improved urinary sodium excretion.

African-Americans are sensitive to stress-related hemodynamic changes. The clinical manifestations may be silent in young age, but this should not deter early diagnosis and treatment. Despite progress, there is a continuing need for additional study. Future studies need to consider investigating some potentially important factors such as obesity, insulin resistance, sex, family history of hypertension, ongoing background stress and their interaction with stress-induced hypertension. Larger studies with longer tracking trials are needed to test whether ARB therapy in young adult African-Americans at risk of stress-induced hypertension will also attenuate long-term cardiovascular morbidity and mortality?

Conflict of Interest: The author declares no conflict of interest and that no funds were received for the preparation of this manuscript

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