ORIGINAL RESEARCH

THE VARIATIONS IN ALTITUDE PREDICT ANGIOTENSIN II AND BLOOD PRESSURE VARIABLES IN JORDAN

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Submitted on: 18.04.18; Revised on: 25.05.18; Accepted on: 06.06.18

ABSTRACT:

Living at high altitudes may be associated with some changes in vascular parameters including blood pressure and angiotensin II. The objectives of the present study were to determine the level of blood pressure in three areas with varying altitudes (Dead Sea, Sea level, and Ajloun), and to determine the level of angiotensin II among participants from the same areas. The methodology involved physical measurement of weight, height, BMI, waist circumference, SBP, DBP, MBP, pulse/min, and PCV. Angiotensin II was measured by ELISA. Data were represented as means and standard deviation. The relationships between variables were examined using independent T test. Study findings showed that there were no significant differences between the means of age, weight, height, BMI, and waist circumferences among participants in study areas ($p>0.05$).the mean of each of SBP, DBP, MBP, pulse/min, and PCV was significantly lower in the Sea Level compared with Ajloun ($P<0.05$).the level of angiotensin II was the highest in participants from Ajloun (12.08±5.19), followed by Sea level (11.21± 6.05), and Dead Sea (8.84 ± 4.65). The difference in mean was only statistically significant between Dead Sea and Ajloun ($p=0.039$). Taken together, blood pressure, the concentration of angiotensin II and PCV were increasing as going toward high altitude (Ajloun) and declining as going toward low altitude (the Dead Sea).

KEYWORDS: Blood pressure, Angiotensin II, Ajloun, Dead Sea, Sea level

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Indian Research Journal of Pharmacy and Science; 17(2018)1449-1455;
Journal Home Page: https://www.irjps.in
DOI: 10.21276/irjps.2018.5.2.7

INTRODUCTION

Blood pressure means the force exerted by the blood against any unit area of the vessel wall (1); this force pushes blood to the different parts of the body to supply nutrients to the tissues and remove waste products away, i.e. to maintain homeostasis in all tissue fluids of the body for optimal survival and function of the cells (2). Blood pressure develops normally in the left ventricle during the systolic part of the cardiac cycle (3). Blood flow through the blood vessel depends mainly on the pressure gradient, which is the force that pushes the blood through the vessel (P= F X R), whereas, P is pressure gradient, F is blood flow; R is the resistance (2). Arterial blood pressure is regulated within a narrow range by baroreceptors to provide adequate perfusion of the tissues without causing damage to vascular system, particularly the arterial intima (4). Mean arterial BP is a function of cardiac output (CO) and total peripheral vascularresistance (TPR) (5) and, in mathematical terms, at constantCO, BP =CO X TPR. CO, in turn, is directly related to ECF volumeand the volume of the venous return to the heart. Indeed, Borstand Borst-de Geus (6) and Guyton and colleagues (7, 8) observedthat acute plasma volume expansion elevates the BP by increasingCO. mostpatients with chronically elevated BP have a relatively normalCO and significantly elevated TPR(9,10). Accordingto Guyton, the tissue overperfusion is an abnormal condition,and TPR, therefore, increases until tissue perfusion returnsto normal. One explanation is that this autoregulation is controlledby the metabolic demands of the tissues (9,7,11).

Angiotensin is an oligopeptide in the blood that causes vasoconstriction, increased blood pressure, and release of aldosterone from the adrenal cortex. It is derived from the precursor molecule angiotensinogen, a serum globulin produced in the liver and it plays an important role in the renin-angiotensin-aldosterone system. Angiotensin was independently isolated in Indianapolis and Argentina in the late 1930s (as 'Angiotonin' and 'Hypertensin' respectively) and subsequently characterized and synthesized by groups at the Cleveland Clinic and Ciba laboratories in Basel, Switzerland (12).

Angiotensinogen is an α-2-globulin that is produced constitutively and released into the circulation mainly by the liver (13). It is a member of the serpin family (serine protease inhibitor)-family of proteins in blood interacts with and inhibits other enzymes of the blood coagulation system (14), although it is not known to inhibit other enzymes, unlike most serpins. Plasma angiotensinogen levels are increased by plasma corticosteroid, estrogen, thyroid hormone, and angiotensin II levels. Angiotensinogen is also known as renin substrate. Human angiotensinogen is 452 amino acids long, but other species have angiotensinogen of varying sizes. The first 12 amino acids are the most important for activity, they are:

Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile

Angiotensin I

Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu

Angiotensin I is formed by the action of renin on angiotensinogen. Renin cleaves the

peptide bond between the leucine (Leu) and valine (Val) residues on angiotensinogen,

creating the ten amino acid peptide, angiotensin I.

Angiotensin I appears to have no biological activity and exists solely as a precursor to angiotensin 2.

Asp-Arg-Val-Tyr-Ile-His-Pro-Phe

Angiotensin I is converted to angiotensin II through removal of two terminal residues by the enzyme Angiotensin-converting enzyme (ACE), which is found predominantly in the capillaries of the lungs (13). ACE is actually found all over the body, but it has its highest density in the lung. Angiotensin II acts as an endocrine, autocrine/ paracrine, and intracrine hormone (15).

Study objectives

- To determine the level of blood pressure in three areas with varying altitudes (Dead Sea, Sea level, and Ajloun), and
- To determine the level of angiotensin II among participants from the same areas.

METHODS AND SUBJECTS

This study was carried out in the Jordan University of Science and Technology-Department of Physiology in the period between October/2008 and May/2009. It covered three areas: the Dead Sea area, sea level, and high altitude area (Ajloun). 500 subjects from each area were involved in the study; all of them were males, apparently healthy, and the same age. The study included two tasks: first, the measurement of

blood pressure and all variables affecting it such as weight, height, waist circumference, in addition to the measurement of heart rate per minute. Second, blood samples were taken from 30 subjects in each area so as to measure the concentration of angiotensin II and PCV.

Blood pressure measurements

Blood pressure was taken for 500 subjects in each target area; it was taken from the right arm of the subject, in a sitting position and after resting for 5 minutes. Blood pressure was taken by sphygmomanometer with a stethoscope.

Measurement of height

Height was measured for our subjects by using 2 metric scaled rulers fixed to the wall of the room. It was in centimeters.

Weight measurement

Weight was measured for all subjects using a well calibrated scale.

Waist circumference measurement

Waist circumference was measured by a manual metric scale in centimeters.

Heart rate measurement

Radial pulse from the left hand for full minute, the subjects were at rest.

Angiotensin II measurement

The principle of this enzyme immunoassay (EIA) is based on monoclonal anti-body. Angiotensin II is immobilized on a 96 well plate. After immunological reaction with Angiotensin II and washing, the trapped molecule is covalently linked to the plate by glutaraldehyde via amino groups. After washing and denaturing treatment, Angiotensin II can react again with the acetylcholinesterase-labelledmAb which is used as tracer. The plate is then washed and Ellman's reagent (enzymatic substrate for AChE and chromogen) is added to the wells. The AChE tracer acts on the Ellman's reagent to form a yellow compound. The intensity of the color, which is determined by spectrophotometry, is proportional to the amount of tracer bound to the well and is proportional to the amount of Angiotensin II.

DATA ANALYSIS

Data were represented as means and standard deviations. Independent T test was used to investigate the relationship between variables. Significance was considered at $p \leq 0.05$.

RESULTS

General characteristics of participants (Dead Sea and Ajloun)

As it can be seen in table 1, the mean age of participants from Dead Sea was 17.60±0.51 years, and this was slightly lower than that of participants at Ajloun area (17.83±0.69 years). The difference in means was not statistically significant ($p>0.05$). The mean weight of participants from Dead Sea was 67.31±10.77 kg and this was slightly less than that of Ajloun 67.37±10.76 kg. No significant differences were observed ($p>0.05$). No significant variations in means were observed for height, BMI, and waist cir for participants from the two study areas.

Table 1: General characteristics of participants

Variables	Dead Sea	Ajloun	P value
	Mean ± std	Mean ± std	
Age	17.60 ± 0.51	17.83 ± 0.69	NS
Weight/kg	67.31 ± 10.77	67.37 ±10.76	NS
Height/cm	169.29 ± 6.52	169.51±7.42	NS
BMI	23.45 ± 3.27	23.42 ± 3.22	NS
Waist cir./cm	76.37 ± 10.26	75.99 ±10.21	NS

Clinical variables associated with participants from Dead Sea and Ajloun

As demonstrated in figure 1, participants from Dead Sea had significantly levels of SBP, DBP, MBP, Pulse/min, and PCV lower than participants from Ajloun ($p<0.05$).

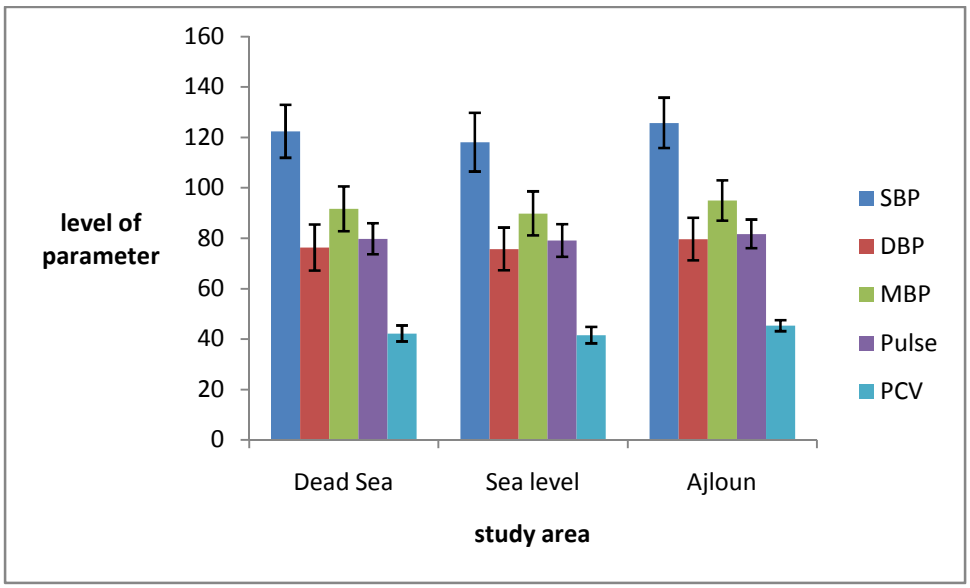

Figure 1: Clinical variables associated with study participants

General characteristics of participants (Sea level and Ajloun)

Table 2 shows the general characteristics and their statistical relationship in Sea level and Ajloun. The results showed that the means of age, weight, height, BMI, and waist were similar among participants from included areas. No significant differences were observed between variables among participants from the study areas (p>0.05 for all variables).

Table 2: General characteristics of participants (Sea level and Ajloun)

Variables	Sea level	Ajloun	P value
	Mean ± std	Mean ± std	
Age	17.60 ± 0.51	17.83 ± 0.69	NS
Weight/kg	67.69 ± 8.70	67.37 ±10.76	NS
Height/cm	170.50± 5.85	169.51±7.42	NS
BMI	23.26 ± 2.57	23.42 ± 3.22	NS
Waist cir./cm	76.38 ± 6.00	75.99 ±10.21	NS

Clinical variables associated with participants from Sea Level and Ajloun

As seen in figure 1, the mean of each of SBP, DBP, MBP, pulse/min, and PCV was significantly lower in the Sea Level compared with Ajloun (P<0.05).

The level of Angiotensin II among participants in study areas and its statistical significance

As seen in table 3 and figure 2, the level of angiotensin II was the highest in participants from Ajloun (12.08±5.19), followed by Sea level (11.21± 6.05), and Dead Sea (8.84 ± 4.65). The difference in mean was only statistically significant between Dead Sea and Ajloun (p=0.039).

Table 3: The level of Angiotensin II among participants in study areas and its statistical significance

Target Area	Mean ± std	Target Area	Mean ± std	P value
Dead Sea	8.84 ± 4.65	Sea level	11.21± 6.05	NS
Ajloun	12.08 ± 5.19	Dead Sea	8.84 ± 4.65	0.039*
Sea level	11.21± 6.05	Ajloun	12.08 ± 5.19	NS

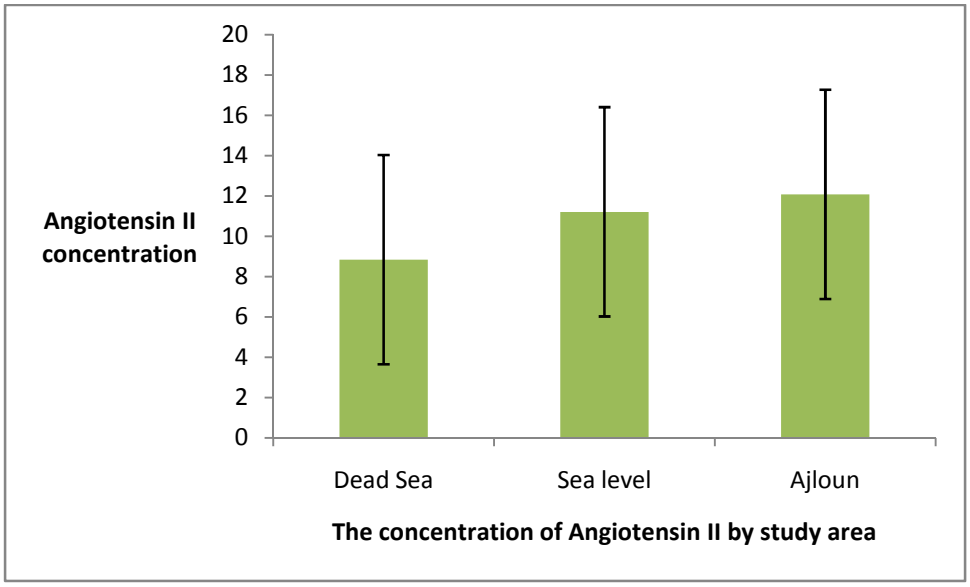

Figure 2: The mean level of angiotensin II in study area

DISCUSSION

The results of this study show that the values of SBP, DBP, MBP, PCV and heart rate in the high altitude area (Ajloun) are higher than the results of the same variables when compared with the Dead Sea area since the p value for all above mentioned variables is highly significant (p value =0.000), the same is when comparing the high altitude area (Ajloun) with the sea level area, it shows that the values of SBP, DBP, MBP, PCV and pulse rate in the high altitude area (Ajloun) are higher than the results of the same variables when compared with the sea level area (p value =0.001).

The comparison between the high altitude, sea level area and the Dead Sea area has revealed that blood pressure, pulse rate and PCV becomes higher as we go from low altitude areas toward high altitude areas. Our results, however, are compatible with those of a study which has been performed in Abha, Saudi Arabia by the department of physiology in King Saud University in which they have tested the effect of altitude on blood pressure in the Assir province of Saudi Arabia (16) and it is also comparable with most of the international studies which have been carried out to clarify the effect of high altitude on blood pressure. The explanation of higher blood pressure in high altitude is that both the direct and indirect effects of the hypoxia are likely to contribute to causing the increase in sympathetic activity at high altitude. Hypoxia acts on vascular smooth muscle in the systemic circulation causing relaxation and therefore hypotension. This, in turn, will lead to baroreceptor-mediated sympathetic excitation. An additional mechanism for exciting sympathetic activity may also arise through stimulation of pulmonary arterial baroreceptors.

Since our subjects are residents of the three target areas, the residents in the high altitude area (Ajloun) are expected to be acclimatized and to have the same

blood pressure and heart rate in comparison with sea area residents (17). This explanation is justified by the fact that chronic high-altitude hypoxia leads to relaxation of vascular smooth muscle in a manner similar to autoregulation or via an increase in collateral circulation .One such example is Cerro de Pasco a busy mining town of 72,000 populations at 4,300 m above sea level in the Peruvian Andes, in which the people live with normal vital signs and with no apparent adverse effects (18). Whereas, in our study, the residents were not able to acclimatize, as shown in our findings.

The results show that the concentration of angiotensin II has been the highest at high altitude and it declined as we went down to the Dead Sea area (p value ≤ 0.05). Returning to what has been written in literature review there has been no any article compatible with our results because angiotensin II has never been measured before.

CONCLUSIONS

This study shows that blood pressure, the concentration of angiotensin II and PCV were increasing as going toward high altitude (Ajloun) and declining as going toward low altitude (the Dead Sea).

It is suggested that blood pressure was higher in Ajloun due to hypoxia in such area of low barometric pressure, while blood pressure was lower in the Dead Sea area (high barometric pressure) which is enriched with oxygen.

ACKNOWLEDGEMENT

The research was funded by Jordan University of Science and Technology. Fund no. 454272.

The research was approved by Jordan university of science and technology committee for human study and a signed consent form was obtained from each participant to participate in the study according to the Institutional Review Board committee.

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CONFLICT OF INTEREST REPORTED: NIL ; SOURCE OF FUNDING: Fund no. 454272/ Jordan University of Science and Technology