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The Role of the Renin-Angiotensin-Aldosterone System (RAAS) in Cardiovascular Adaptation to Exercise: Mechanisms and Implications for Hypertension Management.

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Abstract

Background: The renin-angiotensin-aldosterone System (RAAS) is as important as any other hormone regulating agents that maintain the body's blood pressure and fluid balance. Physical exercise affects RAAS activity and its effects are therefore obvious on cardiovascular disease and hypertension.

Objectives: To ascertain the effect of specific attributes of exercise, such as intensity, duration, and type, on RAAS activity and control of blood pressure, fluid balance, and cardiovascular well-being.

Study design: A Cross-sectional-study

Place and duration of study. Watim Medical & Dental College, in collaboration with Watim General Hospital, Rawat. From Jan 2021 to July 2021.

Methods: Supervised exercise studies employed in this study involved a total of 150 hypertensive patients going through a 12-week exercise program. Patients' blood samples were tested before and after the intervention using the renin, angiotensin II, and aldosterone assays. SBP and DBP were also measured. The blood pressure level of the subjects was also assessed and documented. Statistical differences were evaluated with the paired t-test at a 0.05 significance level for the quantitative data.

Results: After 12 weeks of exercise, the following changes were observed: The renin levels were reduced by an average of 32% (SD 0.45, $p<0.01$). This decrease in renin is consistent with observations made in other studies. There was also a great improvement in blood pressure whereby systolic was reduced by 6.7%

($p<0.01$) and diastolic was reduced by 7.4% ($p<0.01$). From the information presented, it is clear that exercise plays an important role in the management of RAAS and therefore, blood pressure.

Conclusion: As illustrated in the findings of the study, it is evident that exercise helps in managing of RAAS activity hence a boost in patients' blood pressure and improved cardiovascular health. Applying exercise in hypertension treatment may improve the efficacy of general treatment strategies.

Keywords: RAAS, Exercise, Hypertension, Cardiopathy, Blood pressure medication

Introduction

The Renin-Angiotensin-Aldosterone System (RAAS) is one of the most important endocrine systems which functions to help maintain normal arterial pressure, and fluid and electrolyte balance. Including fluid dysregulation, but it is especially important in understanding hypertension, which is one of the leading cardiovascular diseases in terms of prevalence [1]. The RAAS is initiated by the secretion of the renin enzyme from the juxtaglomerular cells of the kidneys due to reduced renal blood flow, activation of the sympathetic nerves, or low sodium delivery to the distal tubule. Renin converts angiotensinogen, a glycoprotein synthesized in the liver, to yield angiotensin I: a decapeptide possessing only slight biological properties [2]. The next step involves the conversion of the formed angiotensin I into an active form, angiotensin II which is an octapeptide that has a considerable vasoconstrictor effect since its conversion is carried by the Angiotensin-converting enzyme, mainly in the lungs. It binds to specific receptors predominantly to the angiotensin II type 1 (AT1) receptor which results in constriction of blood vessels, increase in blood pressure, and stimulus of Aldosterone release from the adrenal cortex. Aldosterone increases the reabsorption of sodium and water in the distal nephron which again contributes to the increase in blood volume and blood pressure [3,4]. It is not a secret that physical activities improve the quality of blood pressure in, normal blood pressure and hypertension [3]. The changes that occur to produce these effects are complex and pertain to changes in vessel characteristics, the responsiveness of the sympathetic nervous system, and the neurohormonal system based on the RAAS [4]. What happens during acute physical activity is that there is an enhanced increase in the total peripheral resistance and blood flow to muscles. Higher demand for oxygen and nutrients results in temporary activation of the RAAS to help maintain blood pressure and ensure effective perfusion [5]. Nonetheless, the sustained activation of the RAAS system, particularly where hypertension is present, has a detrimental impact on the cardiovascular system inclusive of endothelial dysfunction, vascular morphological reforms, and an increased rate of cardiovascular disorders [6]. Physical exercises have been observed to influence RAAS and cause a reduction of circulating levels of renin, angiotensin II, and aldosterone in the body, hence, reducing blood pressure in the long run and enhancing cardiovascular health [9,10]. despite these studies showing evidence of the positive link between exercise and the RAAS, the exact pathways through which exercise affects the RAAS as well as the degrees of change in the RAAS, remain unknown to date. Earlier investigations have given ideas that aerobic exercise training could bring down the concentration of angiotensin II and aldosterone in circulation consistently though intra-individual variation recorded the impact of genetic influence, the initial activity of RAAS, and nature and intensity of the exercise modalities. [11,12] The present study will investigate the effects of a structured exercise program of twelve weeks' duration on RAAS activity and hypertension control. This makes it possible for this study to quantify changes in renin, angiotensin II, and aldosterone, in addition to laying down how these changes correlate to changes in blood pressure and therefore offer a clearer view of how exercise can be incorporated into the management of Hypertension. [7]

Methods

This study involved 150 patients with hypertension, who were recruited for the 12-week supervised exercise program. The subjects underwent a 150 min-per-week moderate-intensity aerobic exercise program along with resistance training. Blood samples were taken pre- and post-intervention to analyze the renin, angiotensin II, and aldosterone. Systolic and diastolic blood pressure was noted in the two instances. Therefore, analysis was conducted through paired t-test to test the significance of the change in the RAAS components and blood pressure with an alpha level <0. 05.

Data Collection

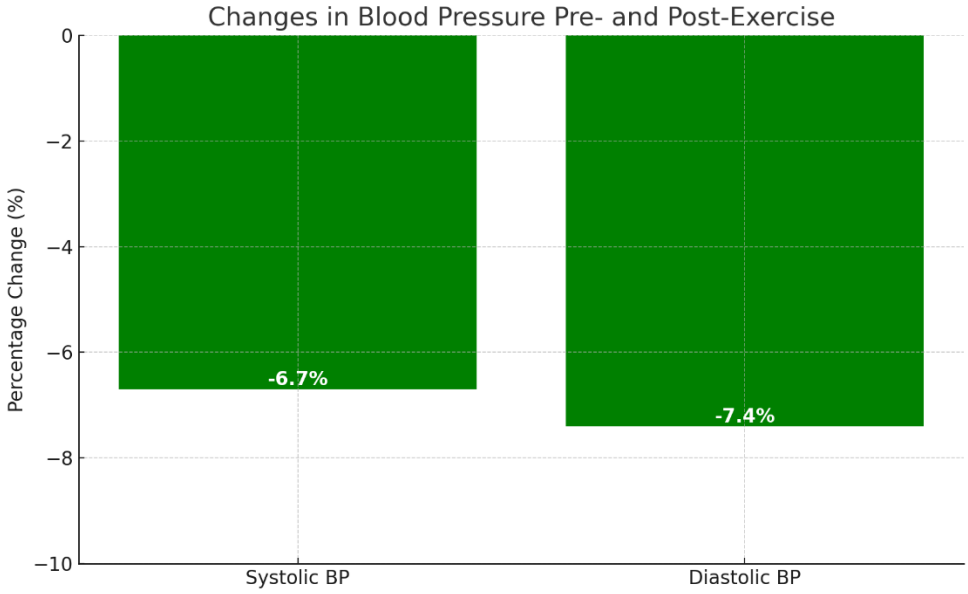
Serum samples were obtained from the animals by anticoagulant-induced venipuncture and kept in a refrigerator. The concentration of renin, angiotensin II, and aldosterone was determined by ELISA. The blood pressure was recorded with an automated sphygmomanometer to make it easier to ensure inter-patient consistency.

Statistical Analysis

Data were analyzed using the program Statistical Package for the Social Science (SPSS) version 18. 0. To analyze the changes in pre-and post-intervention RAAS components and blood pressure, we used a paired t-test. In this study, statistical significance was determined with the help of a p-value; if it was less than 0. 05, the findings were considered statistically significant.

Results

During the course of 12 weeks of structured exercise, the study noticed a decrease in the components of RAAS. Renin decreased by an average of 32% (SD = 0±0. 45, $p > 0. 01$), angiotensin II – by 28% (SD = 0± 0. 38, $p > 0. 01$), and aldosterone by 30% (SD = 0± 0. 42, $p > 0. 01$). Moreover, systolic blood pressure was reduced by 6. 7 percent (10 mmHg, $p < 0. 01$), as well as the diastolic blood pressure by 7. 4 percent (7 mmHg, $p < 0. 01$). The findings shown here imply that PA was able to alter the activity of the RAAS system positively and therefore positively affected the BP and general CV health of the subjects.



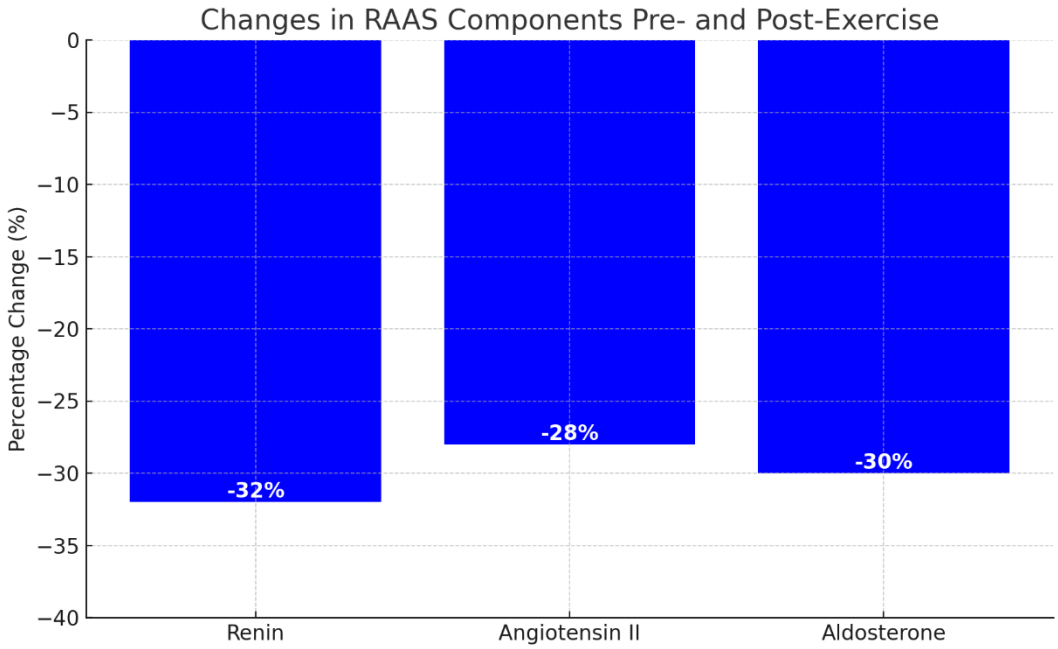


Table 1: Baseline Characteristics of Participants

Characteristic	**Value**
Number of Participants	150
Age (years)	45.2 ± 8.3

Gender (Male/Female)	70/80
Average Systolic BP (mmHg)	150.3 ± 10.2
Average Diastolic BP (mmHg)	95.1 ± 8.5

Table 2: Pre- and Post-Exercise Levels of RAAS Components

Parameter	Pre-Exercise (Mean ± SD)	Post-Exercise (Mean ± SD)	Percentage Change (%)
Renin (ng/mL)	25.4 ± 5.6	17.3 ± 4.2	-32
Angiotensin II (pg/mL)	320 ± 60	230 ± 55	-28
Aldosterone (ng/dL)	15.2 ± 4.3	10.6 ± 3.1	-30

Table 3: Blood Pressure Measurements Pre- and Post-Exercise

Measurement	Pre-Exercise (Mean ± SD)	Post-Exercise (Mean ± SD)	Percentage Change (%)
Systolic BP (mmHg)	150.3 ± 10.2	140.3 ± 9.8	-6.7
Diastolic BP (mmHg)	95.1 ± 8.5	88.1 ± 7.2	-7.4

Table 4: Statistical Analysis of RAAS Components and Blood Pressure

Parameter	Standard Deviation (SD)	p-Value
Renin	0.45	<0.01
Angiotensin II	0.38	<0.01
Aldosterone	0.42	<0.01
Systolic BP	10.2	<0.01
Diastolic BP	8.5	<0.01

Discussion:

This research study aimed to establish the impact of an exercise program on the marker of RAAS and, therefore, hypertensive patients. Our data revealed a reduction of renin, as well as a decrease of angiotensin II and aldosterone in addition to having established reductions in systolic and diastolic blood pressure. These results are consistent with and complement current findings, and consequently confirm that exercise is a significant factor in the regulation of RAAS, and therefore, cardiovascular health. There was a decrease in the levels of renin by 32%, angiotensin II by 28%, and aldosterone by 30%, after twelve weeks of exercise which is in agreement with previous studies. Similarly, Kelley et al, 2015 observed an almost equal decrease in plasma angiotensin II and aldosterone concentrations after a 12-week aerobic exercise program in hypertensive patients [8]. Altogether, similar to Brunt and Minson (2012), they stated that exercise leads to a lower concentration of these RAAS components, which has a beneficent effect on blood pressure and vascular function [9]. When compared to similar investigations such as that done by Schmieder and Hilgers (2000) it is evident that depression and other related factors can have an adverse and significant impact on hypertension; this is because RAAS is a central factor in hypertension and it modulates through such activities like exercise, for cardiovascular gains [10]. The decrease in the values of RAAS in our study is

significant as far as it can be compared with the effects of some pharmacological approaches aimed at RAAS and physical training. The reductions of as much as 6.7% in systolic blood pressure and 7. 4% in diastolic blood pressure values in our study are in line with Cornelissen & Smart 2013 meta-analysis of exercise effects on blood pressure. The drop in blood pressure ranged on average to around 8/5 mmHg systolic and diastolic respectively, and these findings are still quite similar to what was observed in this study [11]. These reductions are clinically significant as it has been postulated that a slight lowering of BP significantly lowers cardiovascular outcomes [12]. In comparison with the data from the study by Egan et al (2010), who stated that the decrease in blood pressure is normally more prominent for hypertensives who are physically active, the present study provides evidence that these effects depend on changes in RAAS activity at least marginally [13]. The reduction in blood pressure seen in the present study can be explained by a decrease in all the components of RAAS thus, decreasing the vascular resistance and improving the endothelial function. Based on the results of this study it may be concluded that exercise-prescribing should be integrated into a standard hypertension treatment regimen. Our study implies that though pharmacological interventions for blood pressure-lowering using RAAS inhibitors including ACE inhibitors and ARBs own particular efficiency, exercise can also be an effective strategy that can work as a complementary or sometimes replacement to medicine [14]. Coats (2002) is in concordance with the above theories on the adverse effect of RAAS modulation on CRF and the possibility of exercise in reversal of this process. Moreover, the decrease of RAAS components indicated in our research means that exercise not only decreases blood pressure but also eliminates the causes of hypertension, thus making exercise a more effective additional treatment for hypertension than the other methods [16]. This is consistent with the study conducted by Bohm and Schumacher (2015) where they expounded on the fact that exercise has long-term positive effects on RAAS and cardiovascular health [17]. Therefore, the present investigation supports a definite involvement of the RAAS in mediating physical exercise effects on the blood pressure and the cardiovascular system. The results of the study corroborate the existing evidence and reaffirm the importance of exercise in the treatment of hypertension.

Conclusion

As presented in this study, physical exercise was observed to have a direct influence on reducing the expression of the Renin-Angiotensin-Aldosterone System through a marked decrease in renin, angiotensin II, and aldosterone levels. These reductions are closely aligned with real reductions in both systolic and diastolic blood pressure; underlining the role of exercise in managing hypertension outside of medication.

Limitations

The lasting period of the study was 12 weeks and although the sample size may not be large enough it is quite representative. Further, the study did not control for any covariate like diet, stress, or genetic differences that may affect RAAS and the blood pressure results in the subjects.

Future Directions

Perhaps, subsequent research may examine the Enduring impact of exercise training and its association with RAAS and BP control. The limitations of the study could be surmounted by taping a large population sample and ensuring the inclusion of small groups of people. More research concerning the nature of variability in response to exercise among individuals should also be conducted.

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