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INCREASE IN CATECHOLAMINE-INDUCED RESPONSIVENESS IN MICROGRAVITY SIMULATED BY HEAD-DOWN MANEUVER IN RATS

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ABSTRACT

Aim/background: Increase in catecholamine-induced responsiveness in microgravity, Simulated by head-down Maneuver in rats were examined on Wistar albino rats in the study. The research was carried out by assessing the activities of epinephrine and dopamine (Catecholamine) on the cardiovascular indices such as systolic and diastolic blood pressure, pulse rats and the mean arterial pressure of the rats by simulating then at head-down Maneuver. **Method:** Groupings were as follows; group I (control), group II (epinephrine-treated), group III (dopamine-treated). And group IV (mixture of groups II and III). Before and after the administration of the drugs (epinephrine and dopamine) and simulated by head- down Maneuver. **Results:** The mean value for the cardiovascular indices investigated were 119. 80± (before infusion of drug and simulation (O min)) and 115. 60± (after infusion of drug and simulation (30 min)) of the control group, 89.40± (O min) and 123. 60± (30 min) of the group II, 117. 40± (O min) and 127.20± (30 min) of the group III and 117.60± (O min) and 124.20± (30min) of the group IV. While that of the dopamine cardiovascular indices and simulated by head- down Maneuver, investigated as following, of its mean value, 116.60±(O min) and 122.80± (30 min) of the control group, 117. 40± (O min) and 156.40± (30 min) of the group II and 127. 60± (O min) and 110.80± (30 min) of the group III. From the results, it was observed that all the test groups had significant increase in their cardiovascular indices when compared with that of the control group. **Conclusion**: During the simulation of by head-down maneuver, there was significant alteration in the systolic and diastolic blood pressure, pulse rate and means arterial pressure of the experimental animals as a result of the decrease in the cardiac outputs in sharp contrast to when treated with the exogenous catecholamine.

KEYWORDS: Catecholamine, microgravity, simulation, head-down maneuver, blood pressure.

INTRODUCTION

Microgravity

Heart Rate Variability (HRV) has been used, during and after exposure to microgravity or its simulation, as a non-invasive tool to monitor autonomic functions.[1,2] It has also been used to assess the efficacy of pharmacological intervention in preventing the effects of increase in the effects of Epinephrine induced by simulated microgravity[3] and to characterize the effect of geomagnetic fluctuations on human body in space[4] Ventilatory parameters have not been controlled/monitored in all these studies. Microgravity results into an increase in respiratory, reduction in tidal volume and dead space. End tidal PCO_2 may also increase due to spacecraft atmospheric conditions.[5]

The human body is a complex innervation of chemical, mechanical and neural pathways designed to allow the body to adapt to situational changes and environmental stressors to maintain homeostasis. By studying the mechanisms behind adaptation, scientists and medical professionals are better able to differentiate between pathological and physiological states, determine control mechanisms and design countermeasures to maintain optimum functionality.[6]

Exposure to microgravity

Whether simulated or actual, has been shown to result in reductions in ventricular mass[7,8], blood volume[8], breathing frequency[9], balance control[10], nervous system sensitivity and reserve[11], arterial tone[12], bone mass[13], immune function[14], muscle mass and space motion sickness[15] This can lead to operational difficulties and health consequences, both in space and upon return to a gravitational body (including Earth or future missions to the Moon/Mars).[15]

The gravity of earth produces a blood pressure gradient that is 70 mmHg at the head and 200 mmHg at the feet in the standing human. However, in microgravity, there is a cephalad fluid shift and an elimination of this gradient, yielding a uniform blood pressure of 100 mmHg throughout the body.[16]

These hemodynamic changes are thought to trigger adaptive changes in the cardiovascular system such that on return to the gravity of Earth, astronauts adapted to microgravity experience cardiovascular deconditioning effects, the most serious of which is orthostatic intolerance.[17] Orthostatic intolerance is a condition in which subjects suffer from lightheadedness, dizziness, palpitations and even syncope on assuming the upright position. Orthostatic intolerance afflicts not only space-flown astronauts but also ~500,000 Americans who experience a chronic form of the syndrome and an even greater population in patients confined to long-term bed rest.[18]

METHODOLOGY

Collection of Experimental Animals

Healthy underweight (80 – 120g) albino rats of the wistar strain was bought from the University of Port Harcourt animal farm Choba campus, Department of Agriculture, Port Harcourt, Rivers state. The animals were fed with rat diets (palletized poultry feeds) and tap water throughout the period of the study (acclimatization and experimental works). The animals was kept three in each compartment of the wire cage.

Acclimatization of Animals

The Wistar albino rats weighing 80-90g was identified and housed in wire mash cage under well ventilated environment of standard conditions 25-29^{o}C respectively. The Wistar albino rats were maintained with rat chow (vital feeds Ltd, Aba) and water ad libitum. The animals were exposed to 12 hours light-dark cycle and handled according to standard protocols. The animals were acclimatized for three (3) weeks at the animal house of the pharmacology department of the University of Port Harcourt. The study was generally conducted in accordance with recommendations from the 1983 declaration of Helsinki on guiding principles in the care and use of animals and accordance with guiding line of the European Convention for the protection of vertebrate animals and other scientific purpose – ETS - 123 (European treating series, 2005).

Simulation of the Albino Wistar Rats during the Fourteen Days

During the acclimatization of the albino Wistar rats, the rats was placed three in each compartment which was labelled group I (control), group II (epinephrine-treated), group III (dopamine-treated) and group IV (dopamine and epinephrine-treated). Simulation was done on all the rats in the four compartment in the interval of fourteen days, only in the morning hours. During simulation the rats were placed in a head-down maneuver in an improvised Head-down Maneuver Box made for six animals.

First to third day of the simulation, the rats was simulated in head-down maneuver for the period of thirty minutes. On the fourth day, still the fourteen day the period of simulation was increased to one hour. After the last day, on the fifteen day, drugs were administered to the rats.

Drugs Administration and Simulation of the Albino Wistar Rats on the Fifteen Day

On the fifteen day the drugs such as epinephrine and dopamine was administered to the rats in dosage such as 0.1ml, 0.2ml and 0.3ml to the group II, III and IV respectively. That of the group I, also known as the control, no drug was administered during the period of the experimental work.

In each of the compartment of the wire cage of the three rats, 0.1ml of epinephrine was injected into two of the rats while the remaining one was injected with 0.1ml dopamine in the group II. In the group III, 0.2ml of epinephrine was injected to two of the rats and 0.2ml dopamine to the other one. In the group IV, 0.3ml of epinephrine was injected to two of the rats and 0.3ml of dopamine to the other one, all through subcutaneous administration. After the injection (administration) of those drugs, they were allowed for the period of 30 minutes before simulation. After the 30 minutes they simulated for the period of one hour.

Blood Pressure Recording After Drug Administration and Simulation.

After the administration of the drugs (epinephrine and dopamine) and allowed for the period of 30 minutes, the animals (rats) was simulated for the period of one hour, after which the blood pressure was taken by the Blood Pressure Recorder machine. The blood pressure record machine, help in recording the systolic pressure (up and down), diastolic pressure (up and down) and their pulse rates. After the first roundup, the albino rats was simulated again for the period of 30 minutes and their blood pressure was taken.

RESULTS

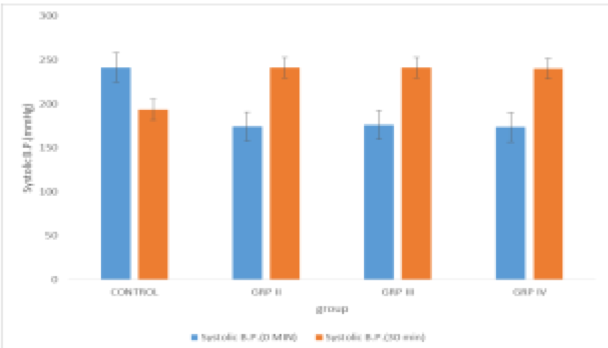

Figure 1: Systolic blood pressure of the albino wistar rats after the administration of the epinephrine and simulated in 30 minutes.

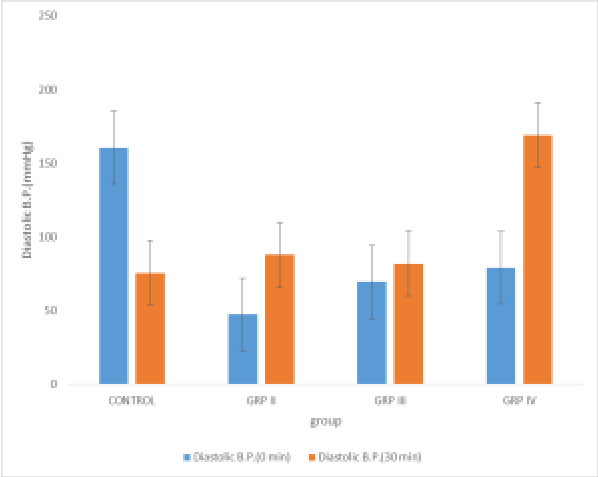

Figure 2: Diastolic blood pressure of the albino Wistar rats after the administration of epinephrine and simulated in 30 minutes.

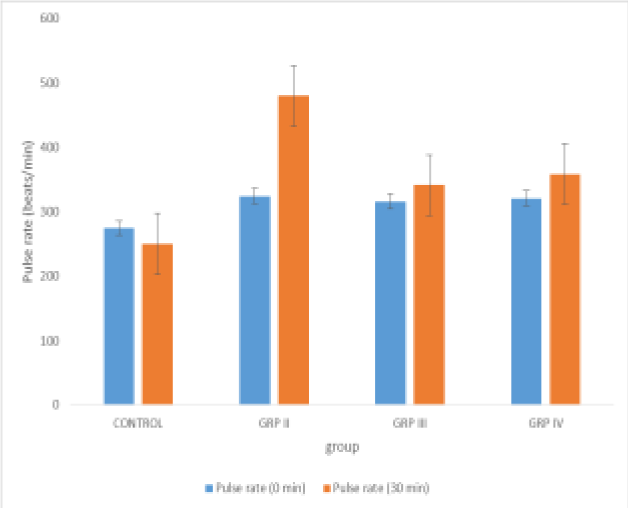

Figure 3: Pulse rate of the albino Wistar rats after the administration of epinephrine and simulated in 30 minutes.

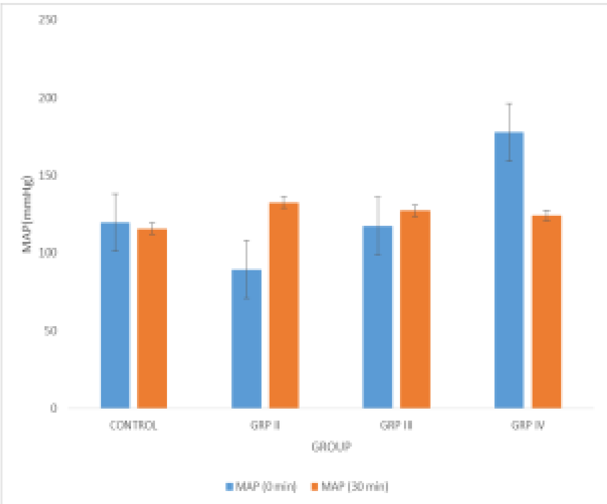

Figure 4: Mean Arterial pressure of the albino Wistar rats after the administration of epinephrine and simulated in 30 minutes.

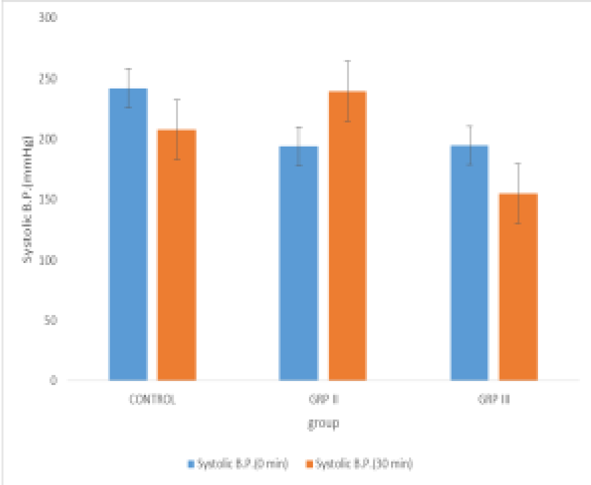

Figure 5: Systolic blood pressure of the albino Wistar rats after the administration of Dopamine and simulated in 30 minutes.

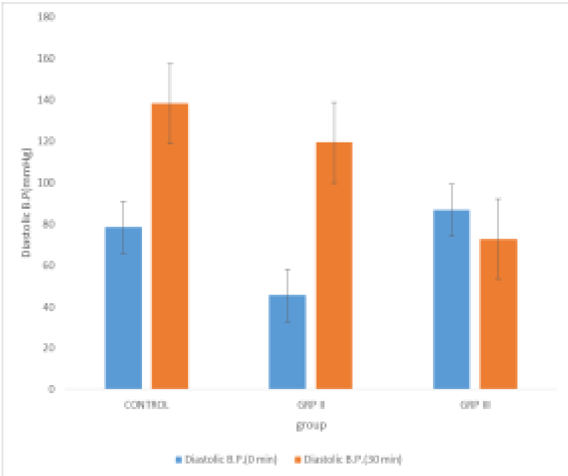

Figure 6: Diastolic blood pressure of the albino Wistar rats after the administration of Dopamine and simulated in 30 minutes.

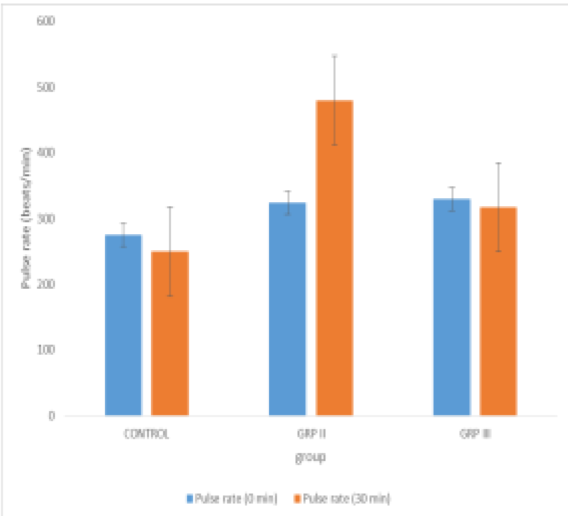

Figure 7: Pulse rate of the albino Wistar rats after the administration of Dopamine and simulated in 30 minutes.

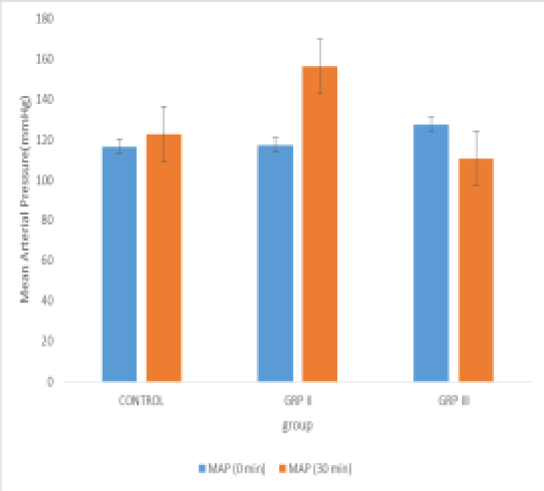

Figure 8: Mean arterial blood pressure of the albino rats after the administration of Dopamine and simulated in 30 minutes.

DISCUSSION

The study was carried out to investigate the effect of catecholamine (epinephrine and dopamine) on the cardiovascular parameters of the albino Wistar rats during or at the state of microgravity by head-down maneuver. The rats were subjected to one (1) month of acclimatization and two weeks (14 days) of simulation by head-down maneuver.

From the results, the systolic blood pressure of the groups II, III, IV tend to increase significantly as a result of an increase in the autonomic output after initial remodeling has occurred[19] increasing systolic blood pressure through an increase in the release of peripheral vasoconstrictors i.e. vasopressin, to maintain homeostasis and preserve cerebral perfusion.[20] Systolic blood pressure remains partially raised to the order of a few mmHg, potentially due the continued lack of inhibitory peripheral nervous system activity and the possible reduced activation of metaboreceptors in muscle afferents, which project type III and IV afferent fibers sending excitatory input to the medulla in the face of robust activation.[21]

The diastolic blood pressure decreased, due to decreased in cardiac input, vasoconstrictions and stiffness of the arterials. (This is in accordance with the works of Grigoriev), after 2 weeks there is a reduction in arterial stiffness and an increase in venous cross sectional area of ~70%[22] consequentially stabilizing and reducing diastolic blood pressure. While in the group II, III and IV, the diastolic blood pressure increased as a result of the stimulation of the drug (epinephrine) on the cardiac (heart) and causes blood vessel relaxation and thereby increase cardiac input and output, this is accordance with work done previously[23] graded Epi-infusion increased heart rate before and during HDBR, the effect being significant starting from the lowest dose of epinephrine. A significant increase in systolic blood pressure was observed but only with the highest dose of epinephrine before HDBR, whereas during HDBR an increase was observed for the two highest doses.

For diastolic blood pressure, no significant effect of Epi was observed before HDBR and a significant positive effect was observed with the highest dose during HDBR[23] contrary in this work diastolic blood pressure tend to decreased in the control and increased in epinephrine induced and significant increase in the highest dose.

From fig. 3, the pulse rate decreased as result of vasoconstriction, low cardiac output and low effect of epinephrine[23] whereas those of the group II, III and IV the pulse rate increased significantly as a result of the effect of epinephrine on the blood vessels (vasodilation) which causes increase in the cardiac input and output, that tend to increase the pulse rate.

The mean arterial pressure in the fig.4, increased due to effect of the epinephrine on the blood vessels, causing then to dilate during the simulation by head-down simulation. This is caused by promoting a sustained reduction of sympathoneural release and a lowering of NE synthesis and turnover and induces a selective increase in β-adrenergic responsiveness in heart[24] and adipose tissue.[25]

These modifications were associated with an increase in Epinephrine-induced changes in plasma glycerol and lactate levels and in energy expenditure during HDBR. These results agree with previous reports from our group[25] and others [24] showing that simulated microgravity promotes an increase in end-organ β-adrenergic pathways. Simulated microgravity increases vasoconstriction and peripheral vascular resistance.

From fig. 5, in the control group, there is decreased in systolic blood pressure after 30 min of head-down simulation. This is in accordance with Goldstein et al, norepinephrine release, synthesis and turnover have been reported during HDBR.[26] Spectral variability of heart rate and systolic blood pressure has been repeatedly shown to be lower during HDBR and spaceflight.[28]

In group II (0.1 mL of dopamine), the systolic blood pressure increased significantly causing the vasoconstriction and increase heart rate via beta receptors and thereby increase the systolic blood pressure from 194.80 $\pm$ 0.49 to 239.40 $\pm$ 0.25.

In the group III, the systolic blood pressure decreased significantly as a result of the increase in dose (0.2 mL of dopamine). This as a result of the increase in the vasodilatation in the mesentery and constriction of the peripheral vessels.

Fig.6, the diastolic blood pressure of the control group and the group II increased significantly whereas that of the group III decreased. According to the Medical

Essential physiology written by Sembulingam et al. 2010, page 424 7th edition and dopamine does not affect the diastolic blood pressure.

From fig.7, the pulse rate of the control group and that of the group II increased significantly. This is in accordance with Goldstein et al, norepinephrine release, synthesis and turnover have been reported during HDBR[26,27] and the increase is as a result of the infused dopamine, caused the vasoconstriction. The group III decreased significantly, which, as a result of the high dose of the drug (dopamine) increased the cardiac output and peripheral vessels constriction.

The mean arterial pressure in the fig.8, increased due to effect of the dopamine on the blood vessels, causes then to constrict and dilate the mesentery vessels during the simulation by head-down simulation. This is caused by promoting a sustained reduction of sympathoneural release and a lowering of NE synthesis and turnover and induces a selective increase in β-adrenergic responsiveness in heart[24] and adipose tissue.[25]

CONCLUSION

In conclusion, this study shows that a short-term HDBR induces an increase in adrenergic responsive,[24] It was equally found that a 14-day HDBR induced an increased β-AR responsiveness. It is an experimental model that provides useful information for an understanding of the autonomic disturbances observed in patients with autonomic failure characterized by loss of sympathetic activity and an increased response to sympathomimetic amines. In addition, the increment of β-adrenergic responses found, even during short-term periods of simulated microgravity (and during space travel), would also explain the autonomic disturbances occurring on return to normal gravity. Indeed, clinical pharmacological interventions with adrenergic drugs acting on SNS and/or peripheral adrenergic receptors may be of major importance in the correction of these troubles.

During the simulation of by head-down maneuver, there was significant alteration in the systolic and diastolic blood pressure, pulse rate and means arterial pressure of the experimental animals as a result of the decrease in the cardiac outputs. But as the drugs (epinephrine and dopamine) are infused, they stimulate the increase in the systolic and diastolic blood pressure, pulse rate as a result of the increase in the cardiac output. The epinephrine and dopamine stimulate the heart and increase the heart rate, raise blood pressure, contract small blood vessels, release sugar stored in the liver and relaxes certain involuntary muscle while contract others. These changes enable the rats to spend more time after the administration of the drugs than before the administration of the drugs.

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