ORGAN FLUID COMPARTMENTS IN RATS EXPOSED TO HIGH ALTITUDE

S.C. JAIN, S.B. RAWAL, H.M. DIVEKAR AND H.S. NAYAR

Defence Institute of Physiology and Allied Sciences
Delhi Cantt-110 010

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Summary : Rats were exposed to acute hypobaric hypoxia corresponding to an altitude of 6,100 m for 5 hours and 24 hours and were studied for organ fluid changes. Total water and extracellular water content of various organs, i.e. lung, liver, spleen, heart, kidney, muscle, brain, testis and subcutaneous tissue were determined by the difference of dry and wet weights and using radiobromide-82 respectively. Lung and liver were found to be significantly hydrated with lower water contents in subcutaneous tissue, spleen and muscle on prolonged exposure. The data indicated a shift of fluids from extracellular to intracellular compartment.

Key words : high altitude body water extracellular water intracellular water

INTRODUCTION

The loss in body weight attributed to body hypohydration on abrupt high altitude exposure has been a well-observed phenomenon. Changes in organ weights of rats exposed to actual and simulated altitudes have been reported by several investigators (7,8,11,12), but their findings are not in agreement. Christensen *et al.* (3) reported the shift of fluids from extracellular to intracellular compartment in the various organs as shown by the electrolyte balance studies. However, no report on the direct measurement of extracellular as well as intracellular water content of various organs of animals exposed to high altitude is available. Taking into consideration the above facts, an attempt has been made to study in detail the extracellular and intracellular water content of various important organs of animals on acute altitude exposure.

MATERIALS AND METHODS

The subjects for this study was thirty-six healthy albino rats weighing 200 to 250 *g* each. These rats were divided in three groups, namely, (i) control, (ii) exposed to hypobaric hypoxia for 5 hours and (iii) exposed to hypobaric hypoxia for 24 hours. The hypoxic exposure was given in a hypobaric chamber maintained at ambient room temperature and pressure corresponding to an altitude of 6,100 m.

Total body water content was determined by observing the difference of dry and wet weight of the various organs and tissues. Bromide space as measured by radiobromide, $NH_4{}^{82}Br$ is taken to be a representative of extracellular water content in different organs (1). Twenty μCi of the radioactive material, made to 1 *ml* by diluting with 0.9% sterile saline solution with 0.2 *ml* air bubble was injected intramuscularly in the right thigh musc one hour before the termination of the hypoxic exposure. The air bubble has been intro duced in the syringe to make it sure that all the contents in the syringe including needle a delivered to the animal (8). These animals were then put back in the chamber immediate after the radioactive solution injection. Rats were anaesthetized by giving sodium pent barbitol intraperitoneally after the completion of hypoxic exposure. Control rats were giv the similar treatment in an open chamber. About 3 *ml* blood was drawn in a heparinis syringe by cardiac puncture. A maximum amount of blood was drawn by cutting t dorsal aorta. The lung, liver, heart, spleen, left thigh muscle, left kidney, left testis a subcutaneous tissue from the abdomen were excised and superficial fascia and fat we removed. Major cavities and important blood vessels of the organs were gently pressed remove blood. The tissue surface was blotted with filter paper and the wet weight w recorded. The brain was removed after cutting across the frontal bone and removing t frontal, parietal and interparietal bones and weighed immediately. All organs and tissu were counted in a gamma-ray spectrometer and compared with counts of 1 *ml* plasma t give extracellular water content of the organs. All organs and tissues were then dried t constant weight in an oven at about 105°C and weighed to the nearest milligram. Intra cellular water content of the organ was calculated from the difference of total water a extracellular water content.

RESULTS

Table I summarised the total water content of various organs and tissues of ra divided in three groups, namely, (1) control, (2) exposed to acute hypobaric hypoxia f 5 hours and (3) exposed to acute hypobaric hypoxia for 24 hours. Lung and liver we significantly hydrated by 5 hr of altitude exposure and there had been further margin hydration on exposure of longer duration i.e. 24 hours; the increase in lung and liver bei 1.6% ($P<0.01$) and 4.2% ($P<0.005$) after 5 hours and 1.9% ($P<0.001$) and 4.7% (P< 0.005) after 24 hours respectively. However, heart showed initially hydration to t extent of 1.8% ($P<0.025$) but returned to control level on prolonged exposure. On t other hand, muscle and subcutaneous tissue were significantly hydrated by 3.4% and 3.8 respectively after 5 hours and were further dehydrated on prolonged exposure, the increas being 5.4% and 6.1% in muscle and subcutaneous tissue respectively.

Table II summarised the extracellular water content of various organs and tissu of rats in three groups. Extracellular water content of testis and kidney were significant lowered after 5 hr exposure to hypobaric hypoxia by 25.1% ($P<0.01$) and 10.2% (P<0.0 respectively and prolonged hypoxic exposure of 24 hr duration resulted in slight gain extracellular water content of the two organs, though the level in testis was still significant lower than control value. Liver, subcutaneous tissue and spleen showed an insignific decrease in extracellular water content while lung and muscle showed an insignificant increase after 5 hr altitude exposure. On prolonged hypoxic exposure of 24 hr duration, extracellular water content of liver, subcutaneous tissue and spleen remained insignificantly lowered.

TABLE I : Total water contents ($\mu l/g$) of various organs and tissues on acute altitude exposure.

	Control	*5 hr hypoxia*	*24 hr hypoxia*
Lung	764±3	776±3*	779±3**
Liver	687±4	716±8**	719±9**
Heart	761±4	775±3*	760±4
Subcutaneous tissue	759±5	730±9*	713±11**
Brain	770±5	780±5	780±5
Spleen	748±4	758±5	724±5**
Thigh muscle	754±7	728±9*	713±15*
Testis	850±5	851±5	856±6
Kidney	764±4	773±4	764±4

*$P < 0.05$
**$P < 0.005$

TABLE II : Extracellular water contents ($\mu l/g$) of various organs and tissues on acute altitude exposure.

	Control	*5 hr hypoxia*	*24 hr hypoxia*
Lung	587±7	599±15	596±20
Liver	342±10	319±10	312±18
Heart	350±16	350±14	338±24
Subcutaneous tissue	252±10	230±10	230±19
Brain	156±6	152±8	157±10
Spleen	393±6	374±12	377±19
Thigh muscle	231±15	233±23	235±18
Testis	387±12	290±32*	299±33*
Kidney	522±12	469±21*	488±16

*$P < 0.05$

TABLE III : Intracellular water contents (µl/g) of various organs and tissues on acute altitude exposure.

	Control	5 hr hypoxia	24 hr hypoxia
Lung	178±7	177±16	183±15
Liver	345±12	397±15*	407±18*
Heart	412±16	425±14	422±18
Subcutaneous tissue	507±11	500±15	483±16
Brain	614±10	629±9	623±10
Spleen	355±5	384±15	347±12
Thigh muscle	523±18	495±29	478±21
Testis	463±15	561±30*	557±30*
Kidney	242±12	304±23*	276±20

*$P<0.05$

The intracellular water contents of various organs and tissues of rats are listed in Table III. The intracellular water content of liver, testis and kidney were significantly increased after 5 hr hypoxic exposure, the increase being 15.1% in liver ($P<0.025$), 21.2% in testis ($P<0.01$) and 25.6% in kidney ($P<0.05$). Prolonged hypoxic exposure of 24 hr duration resulted in further increase in intracellular water content of liver but a marginal reducation in testis and kidney. Heart, brain and spleen showed an initial insignificant increase in intracellular water content and the levels are maintained on continued hypoxic exposure except that there is a fall in intracellular water content of subcutaneous tissue and muscle showed a progressive insignificant decrease on exposure to simulated altitude.

DISCUSSION

In the present study, lung, liver and heart were found significantly hydrated within 5 hr of acute altitude exposure with reduced water contents of subcutaneous tissue and muscle. Brain, spleen & kidney were found to be insignificantly hydrated after 5 hr of altitude exposure. Longer hypoxic exposure of 24 hr duration resulted in further loss of water from subcutaneous tissue and muscle with significant dehydration of the spleen. Hydration of heart and kidney returned to normal levels after 24 hr while lung and liver remained significantly hydrated. Christensen *et al.* (3) also observed the liver, spleen, kidney, heart and brain to be initially hydrated but liver found to be only hyperhydrated on prolonged exposure to simulated altitude. The increased hydration of liver in this study could be due to an increased fat content by an impairment of lipid metabolism reported in altitude exposed animals (2). The increased water content of organs are likely to be responsible for increased organ weight to body weight ratios of rats exposed to altitude (13). Timiras *et al.* (12) reported heart, kidney, liver and testis to be hydrated after 24 hr of altitude exposure with reduced spleen water content after 24 hr of hypoxic exposure. Darrow and Sarson (4) also showed an increased kidney and liver weight in rats on acute altitude exposure. An increased water content in the heart and kidney of altitude exposed rats has been previously reported (9,14). On the contrary, Sundstorem and Michaels (11) reported a slight decrease in kidney and liver weight on altitude exposure. The increased blood flow in heart, skeletal muscle and lung on altitude exposure has been reported (15) and may be partially responsible for their increased hydration. Cutaneous blood flow decreases at high altitude, the blood being redistributed as a reservoir of oxygen to the other areas of the body. This may be responsible for decreased hydration of the subcutaneous tissue and muscles in the present study.

Extracellular water content of all organs and tissues except lung were found lowered after 5 hr of altitude exposure. On exposure of longer duration of 24 hr, there is no further change in extracellular water content. The intracellular water contents of liver, testis and kidney were found increased. Christensen *et al.* (3) suggested a shift of fluid from extracellular to intracellular compartments as shown by electrolyte balance studies. Our studies also showed a shift of fluid from extracellular to intracellular compartments in all organs and tissues except subcutaneous tissue and muscles. The different behaviour of subcutaneous tissue and muscles may be due to decreased blood flow in these organs (6,7). Hannon *et al.* (6) have reported a marked recompartmentalization of the body fluids in humans within three days of altitude stay and reported a shift of fluids from extracellular to intracellular compartments. Similar observations were made in rats (2) and in human subjects (5).

The present study confirmed a shift of fluid from extracellular to intracellular compartments. The increased extracellular water content of the lung appears to be responsible for the observed interstitial edema and may lead to high altitude pulmonary edema (HAPO)

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REFERENCES

1. Baratt, T.M. and M. Walser. Extracellular fluid in individual tissues and in whole animals - The distrib of radiosulphate and radio-bromide. *J. Clin. Invest.,* **48** : 56-66, 1969.
2. Chinn, K.S.K. and J.P. Hannon. Effect of diet and altitude on the body composition of rats. *J. Nutr.,* **10** 732-738, 1970.
3. Christensen, B.M., H.L. Johnson and A.V. Ross. Organ fluid changes and electrolyte excretion of rats exp to high altitude. *Aviat. Space Environ. Med.,* **46** : 16-20, 1975.
4. Darrow, D.C. and E.L. Sarason, Some effects of low atmospheric pressure on rats. *J. Clin. Invest.,* **23** : 1 1943.
5. Frayser, R., I.D. Rennie, C.W. Gray and C.S. Houston. Hormonal and electrolyte response to exposure to 17,5 *J. Apl. Physiol.,* **38** : 636-642, 1975.
6. Hannon, J.P. and G.B. Rogers. Body composition of mice following exposure to 4,300 and 6,100 metres. A *Space Environ. Med.,* **46** : 1232-1235, 1975.
7. Heath, D. and D.R. Williams. Man at high altitude : The pathophysiology of acclimatisation and adapta Churchill Livingstone, Edinburgh, p. 268, 1977.
8. Macfarlane, W.V., B. Howard, G.M.O. Maloy and D. Hopcraft. Tritiated water in field studies of ruminant me bolism in Africa. In : Isotope studies of the physiology of Domestic Animals. *Proc. of a Symp; IAEA, Vien* pp. 83-94, 1972.
9. Mc Grath, J.J. and R.W. Bullard. Altered myocardial electrolyte content of high altitude exposed rats. *Am. Physiol.,* **219** : 374-377, 1970.
10. Schnakenbeurg, D.C., L.F. Krabill and P.C. Weiser. The anorexic effect of high altitude on weight gain, nitro retention and body composition. *J. Nutr.,* **101** : 787-796, 1971.
11. Sundstorem, E.S. and G. Michaels. The adrenal cortex in adaptation to altitude, climate and cancer. *Ma Univ. Calif.,* **12** : 1-410, 1942.
12. Tirmiras, P.S., A.A. Krumm and N. Pace. Body and organ weights of rats during acclimatisation to an altitu of 12,470 ft. *J. Physiol.,* **19** : 598-604, 1973.
13. Tucker, A. and S.M. Horvath. Relationship between organ weight and blood flow in rats adapted to simula high altitude. *Aerospace Med.,* **44** : 1036-1039, 1973.
14. Uldall, P.R., W.F. Schorr, J.R. Osmun, D.A. Ogden and J.H. Holmes. Effects of hypoxia, hypotension a acidosis on the electrolyte of rats kidneys. *Nephron,* **7** : 1-14, 1970.
15. Vogel, J.A., R.I. Pulver and T.M. Burton. Regional blood flow distribution during simulated high altitude expos *Fed. Proc.,* **28** : 1155-1159, 1969