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Blood-gas properties of plateau zokor (*Myospalax baileyi*)

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Abstract

Plateau zokor (*Myospalax baileyi*) is one of the blind subterranean mole rats that spend their life solely underground in sealed burrows. It is one of the special species of the Qinghai-Tibet plateau. In their burrows, oxygen is low and carbon dioxide is high and their contents fluctuate with the change of seasons, soil types, rain and depth of burrows. However, plateau zokors show successful adaptation to that extreme environment. In this study, their adapting mechanisms to the hypoxic hypercapnic environment were analyzed through the comparison of their blood-gas properties with that of pikas (*Ochotona curzniae*) and Sprague-Dawley rats. The results indicated that plateau zokors had higher red blood corpuscle counts (8.11 ± 0.59 (10^{12}/L)) and hemoglobin concentrations (147 ± 9.85 g/L), but hematocrit (45.9 ± 3.29%) and mean corpuscular volume (56.67 ± 2.57 fL) were lower than the other rodents. Their arterial blood and venous blood pH were 7.46 ± 0.07 and 7.27 ± 0.07. Oxygen pressure in arterial blood of plateau zokors was about 1.5 times higher than that of pikas and rats, and it was 0.36 and 0.26 times in their venous blood. Partial pressure for carbon dioxide in arterial and venous blood of plateau zokors was 1.5-fold and 2.0-fold higher, respectively, than in rats and pikas. Oxygen saturation of plateau zokors was 5.7 and 9.3 times lower in venous blood than that of pikas and rats, respectively. As result, the difference of oxygen saturation in arterial blood to venous blood was 2- and 4.5-fold higher in plateau zokors as that of pikas and rats, respectively. In conclusion, plateau zokors had a high tolerance to pH changes in tissues, together with strong capabilities to obtain oxygen from their hypoxic-hypercapnic environment.

Keywords: Blind subterranean mole rat; Blood-gas; Hypoxia; Hypercapnia; Plateau zokors (*Myospalax baileyi*); Pikas (*Ochotona curzniae*); Qinghai-Tibet plateau; Sprague-Dawley rat

1. Introduction

The plateau zokor (*Myospalax baileyi*) is one of the blind subterranean mole rats that spend their life solely underground in sealed burrows (Fan and Shi, 1982). Belong to the genus *Myospalax* of the family of Cricetidae, they are distributed extensively in the eastern areas of the Qinghai-Tibet plateau at elevation of 2000–4200 m (Fan and Shi, 1982). Plateau zokor is one of the specialized species of Qinghai-Tibet plateau. The barometric pressure in that area is approximate 500 mm Hg and this factor affects the content of oxygen in burrows of plateau zokors in a certain degree. The study indicated that, in 18 cm depth burrows, the content of oxygen was 18.02%, 17.04% and 18.43% and the content of carbon dioxide was 0.22%, 1.46% and 0.81% in the spring, summer and autumn, respectively (Zeng et al., 1984). The average air temperature is between −4 °C and −8 °C. For a period of 4–6 months, the daily average air temperature is below 0 °C at an elevation of 2000–4000 m. Plateau zokors have to live in a depth of 70–250 cm burrows about 5 months (November to March) because of the effect of low temperature (Fan and Gu, 1981). We suggested that, in the burrows of plateau zokors, the content of oxygen was decreased and carbon dioxide was increased obviously because of poor permeability of freezing soil surface (thickness about 30–40 cm) and the respiration of plateau zokors in winter. Therefore, the fluctuation range of oxygen and carbon dioxide in the burrows of plateau zokors was probably greater. Our studies revealed that plateau zokors showed successful adaptation to their extreme environmental conditions. It is indicated that the red blood corpuscle (RBC), the content of hemoglobin (Hb) and myoglobin (Mb) increased remarkably (Zeng et al.,

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Table 1
Comparison of blood indices of plateau zokors (*Myospalax baileyi*) with that of pikas and rats

Species	n	RBC ($N \times 10^{12}$/L)	Hb (g/L)	HCT (%)	MCV (fL)
Plateau zokor	30	8.11 ± 0.59^b	147 ± 9.85^b	45.9 ± 3.29^a	56.67 ± 2.57^a
Pika	15	8.45 ± 1.37^b	133 ± 18.5^a	44.2 ± 3.14^a	52.34 ± 5.20^a
Rat	15	6.82 ± 0.62^a	151 ± 9.54^b	51.9 ± 2.25^b	76.47 ± 4.83^b

Values are given as mean±S.D. Means with different superscripts are statistically different in the same rank (Duncan's test, $\alpha = 0.05$). Means with superscript a are significantly lower than those with b ($P < 0.05$). RBC, Hb, HCT and MCV represent red blood corpuscle, hemoglobin, hematocrit and mean corpuscular volume, respectively.

1984; Wei et al., 2001a,b), but heart rate (Zeng et al., 1984), the activitiy of lactate dehydrogenase (LDH) and the content of 2,3-bisphosphoglycerate (2,3-BPG) in blood of plateau zokors were decreased markedly compared with pikas (*Ochotona curzniae*), an animal living in the same area with plateau zokors, mice and Sprague-Dawley rats (Zhou et al., 1984; Liu et al., 1985). It is suggested that plateau zokors had special adapting mechanisms to hypoxia-hypercapnia, and the tissues of plateau zokors were not short of oxygen although they live in hypoxic hypercapnic burrows. To explore the adaptation mechanisms of plateau zokors to hypoxia-hypercapnia, their blood-gas properties were analyzed and compared with those of pikas and Sprague-Dawley rats.

2. Materials and methods

2.1. Animals

The plateau zokors and pikas were captured near the Haibei Alpine Meadow Research Station, the Chinese Academy of Sciences (elevation 3200 m). The station is located in northeast of Qinghai-Tibet Plateau at latitude 37°42′N and longitude 101°35′E. The barometric pressure was approximate 508 mm Hg. Pathogen-free Sprague-Dawley (SD) rats (*Rattus norvegicus*) were purchased from the Animal Center of Lanzhou Medicine College (elevation 1500 m). According to the digging burrow habit, the plateau zokors were immediately put into plastic boxes (40 cm × 40 cm × 40 cm) filled with soil of their habitat after captured and brought back to the laboratory. The body mass of the plateau zokors and the SD rats was between 200 g and 250 g and of the pikas was between 150 g and 200 g. All procedures involved in the handling and care of animals were in accordance with the China Practice for the Care and Use of Laboratory Animals and approved by the China Zoological Society.

2.2. Sample preparation

All animals were adapted for 24 h in the laboratory (elevation 2300 m, temperature 20–22 °C). Thirty plateau zokors, fifteen pikas and fifteen SD rats were anesthetized with intraperitoneal injection of sodium pentobarbital (50 mg/kg) and the left neck arterial blood vessel was isolated. The arterial blood was collected from the left neck arterial blood vessel and venous blood was collected from right ventricle with a PREZA-PAK® II arterial blood sampler (Yerumo Corp., Tokyo, Japan) for analyzing blood-gas (pH, PCO_2, PO_2 and SaO_2). The same number of animals were killed by decapitation and blood was collected in tubes containing EDTA-Na_2 for analyzing red blood corpuscle, hemoglobin, hematocrit and mean corpuscular volume.

2.3. Blood analysis

Red blood corpuscle, hemoglobin, hematocrit and mean corpuscular volume were analyzed with a blood indices analyzer (SF-3000, USA). The measurement temperature is regulated to 30 °C by the blood indices analyzer automatically. Blood-gas properties were analyzed with blood-gas analyzer (GEM-3 000, USA). The measurement temperature was set to 37 °C.

2.4. Statistical method

All values were expressed as mean ± S.D. Statistical analysis of results was done by one-way of variance, followed by Duncan's test using SPSS 11.0.

3. Results

Compared with the pikas, the hemoglobin in blood of the plateau zokors was markedly elevated, while the red blood cell count, hematocrit (HCT) and mean corpuscular volume showed no difference. Compared with the SD rats, the plateau zokors had higher red blood corpuscle, but hematocrit and mean corpuscular volume were noticeably lower, while hemoglobin concentration did not differ (Table 1).

In the plateau zokors, the arterial blood pH was higher than that of the pikas and the SD rats, but venous blood pH did not differ. The differences of pH between arterial blood and venous blood in the plateau zokors, the pikas and the SD rats were 0.19, 0.04 and 0.04, respectively (Table 2). The oxygen pressure in arterial blood of the plateau zokors was about 1.5 times higher than in the other two rodent species. In contrast, oxygen partial pressure in venous blood of the plateau zokors was lower, amounting to 0.36 and 0.26 times as much as that of pikas and SD rats, respectively. Carbon dioxide partial pressure in arterial and venous blood of the plateau zokors was higher: it was about 1.5 times higher than in pikas and SD rats in arterial blood, and about 2.0 times higher than in pikas and SD rats in venous blood (Table 3). The saturation of oxygen of the plateau zokors was higher in arterial blood, but lower in venous blood than in the

Table 2
Comparison of blood pH of plateau zokors (*Myospalax baileyi*) with that of pikas and rats

Species	n	pH	
		Arterial blood	Venous blood
Plateau zokor	30	7.46 ± 0.07^a	7.27 ± 0.07
Pika	15	7.34 ± 0.07^b	7.30 ± 0.08
Rat	15	7.38 ± 0.05^b	7.34 ± 0.06

Values are given as mean±S.D. Means with different superscripts are statistically different in the same rank (Duncan's test, $\alpha = 0.05$). Means with superscript a are significantly lower than those with b ($P < 0.05$).

Table 3
Comparison of PCO_2 and PO_2 in blood of plateau zokors (*Myospalax baileyi*) with that of pikas and rats

Species	*n*	PCO_2 (mm Hg)		PO_2 (mm Hg)	
		Arterial blood	Venous blood	Arterial blood	Venous blood
Plateau zokor	30	51.97 ± 12.94^b	76.86 ± 22.91^b	81.25 ± 24.93^b	9.42 ± 3.46^a
Pika	15	36.00 ± 7.43^a	38.40 ± 8.55^a	55.95 ± 11.93^a	25.88 ± 4.35^b
Rat	15	33.68 ± 3.98^a	40.05 ± 6.23^a	59.85 ± 5.33^a	35.75 ± 11.10^c

Values are given as mean ± S.D. Means with different superscripts are statistically different in the same rank (Duncan's test, $\alpha = 0.05$). Means with superscript a are significantly lower than those with b ($P < 0.05$) and the same as b and c. PCO_2 and PO_2 represent partial pressure of carbon dioxide and partial pressure of oxygen, respectively.

other two rodents. In venous blood, the values were as much as 5.7 times and 9.3 times lower than those for pikas and rats, respectively. As result, the overall differences in oxygen saturation in arterial blood to saturation of oxygen in venous blood of the plateau zokors were 2 and 4.5 times higher than for pikas and rats, respectively (Table 4).

4. Discussion

The plateau zokor (*M. baileyi*) is a blind subterranean mole rats that spend their life solely underground in sealed burrows (Fan and Shi, 1982). In the burrows of the blind subterranean mole rats, the contents of oxygen and carbon dioxide fluctuate greatly (Zeng et al., 1984; Arieli, 1979; Kennerly, 1964; Kuhnen, 1986). The minimal carbon dioxide levels and maximal oxygen levels ranged from 7.2% and 6.1%, respectively, in burrows of *S. carmeli* in northern Israel (Shams et al., 2005). Compared to rats (*R. norvegicus*), the ventilation of the blind subterranean mole rats at rest did not respond to moderate hypoxia-hypercapnia, but was increased in extreme hypoxia-hypercapnia (Arieli, 1979). The blind subterranean mole rats showed strong a tolerance to hypoxia compared with the rats. Under laboratory conditions, *Spalax* sp. survived 3% O_2 and up to 15% CO_2 for at least 14 h without any deleterious effects or behavioral changes (Avivi et al., 1999; Shams et al., 2004a,b). However, *Rattus* sp. died after 2–4 h under the same conditions (Avivi et al., 1999). Our study indicated that oxygen pressure (81.25 ± 24.93 mm Hg) in arterial blood of the plateau zokors was about 1.5 times as much as that of the pikas and the SD rats, and that (9.42 ± 3.46 mm Hg) in venous blood was 0.36 and 0.26 times as much as that of the pikas and the SD rats. The saturation of oxygen (94.47 ± 4.34 mm Hg) in arterial blood of the plateau zokors showed no difference compared with that of the pikas and the SD rats, but it (7.65 ± 4.77 mm Hg) was 5.7 times and 9.3 times in venous blood less than that of the pikas and the SD rats, respectively. The difference of saturation of oxygen (86.82 ± 5.53%) in arterial blood to venous blood of the plateau zokors was 2 and 4.5 times that of the pikas and the SD rats, respectively. These results suggested that the plateau zokors had strong capabilities to get oxygen from the hypoxic hypercaonic environment, and their tissues have an abundant oxygen supply.

Results indicated that blind subterranean mole rats have evolved special adaptive mechanisms that include blood properties, anatomical and biochemical changes in respiratory organs, and structural and functional changes in a growing list of genes. Compared to other rodents, lung diffusion capacity of blind subterranean mole rats is markedly increased (Widmer et al., 1997) permitting continued oxygenation of blood to occur in their lung under hypoxic-hypercapnic conditions. The primary structures of hemoglobin of blind subterranean mole rats displayed many amino acid substitutions that probably enhance its oxygen affinity (Kleinschmidt et al., 1984). The increase of hemoglobin and decrease in the 2,3-bisphosphoglycerate of erythrocyte (Ar et al., 1977) enhances the oxygen binding rate of hemoglobin, and the reduction in the mean corpuscular volume (Ar et al., 1977) facilitates oxygen transportation. In the tissues such as the skeletal muscle of the blind subterranean mole rats, the mitochondrial density, the capillary density and myoglobin concentration increased significantly (Arieli and Ar, 1979; Widmer et al., 1997; Avivi et al., 1999). It reduced the diffusion distance of oxygen to the mitochondrial and permitted oxygen delivery efficiently. Similarly, haptoglobin (Nevo et al., 1989) and myoglobin (Gurnett et al., 1984) of some blind subterranean mole rats displayed many amino acid substitutions that probably enhance their affinity for oxygen and high amounts of oxygen can be transported to tissues from blood even at low capillary PO_2. Therefore, the blind subterranean mole rats including plateau zokor, although living in a hypoxic hypercapnic environment, had higher oxygen pressure and oxygen saturation in arterial blood, lower oxygen pressure and oxygen saturation in venous blood, and a higher oxygen utilization rate in tissues than the other rodents.

The adaptation of blind subterranean mole rats to the burrowing environment not only related to the unique physiological but also to the expression of genes related to the respiratory proteins. Hypoxia-inducible factor-1 (HIF-1) is mammalian master regulator of O_2 homeostasis (Wang and Semenza, 1995). HIF-1 regulates expression of numerous genes related to erythropoiesis, angiogenesis, vasodilatation, and genes involved in glycolytic process (Semenza, 1998). Studies have demonstrated that the expression pattern and levels of HIF-1á, *EPO* and *VEGF* mRNA in a blind subterranean mole rat differed from that in rats (Shams et al., 2004a,b; Avivi et al., 1999).

Our results revealed a pH difference between arterial blood and venous blood in plateau zokors of 0.19, a value that is

Table 4
Comparison of SaO_2 in blood of plateau zokors (*Myospalax baileyi*) with that of pikas and rats

Species	*n*	SaO_2 (%)		$SaO_{2(a-v)}$ (%)
		Arterial blood	Venous blood	
Plateau zokor	30	94.47 ± 4.34^b	7.65 ± 4.77^a	86.82 ± 5.53^c
Pika	15	85.26 ± 6.92^a	43.47 ± 9.84^b	43.54 ± 4.85^b
Rat	15	91.23 ± 2.74^b	71.47 ± 8.54^c	19.53 ± 7.25^a

Values are given as mean ± S.D. Means with different superscripts are statistically different in the same rank (Duncan's test, $\alpha = 0.05$). Means with superscript a are significantly lower than those with b ($P < 0.05$) and the same as b and c. SaO_2 and $SaO_{2(a-v)}$ represent degree of oxygen saturation in blood and difference of SaO_2 between arterial blood and venous blood, respectively.

significantly greater than that for pikas and SD rats. We assume that high concentrations of CO_2 resulted in a pH decrease in their venous blood, and high concentration of carbonic acid and salts of carbonic acid increased buffering capacity to CO_2 in arterial blood. It suggests that the plateau zokors possess a high tolerance to pH changes in tissues, which may be due to presence of low-activity anhydrase 1 (CA I) and absence of high-activity carbonic anhydrase 2 (CA II) (Yang et al., 1998). PCO_2 in arterial and venous blood of the plateau zokors were markedly higher: about 1.5 times as much as that of the pikas and the SD rats in arterial blood and about 2.0 times as much as that of the pikas and the SD rats in venous blood, respectively. The increase of PCO_2 in blood decreases the affinity of Hb for oxygen. However, hypercapnia was reported to protect against the damaging effects of ischemia and hypoxia. A significant reduction in brain damage induced by hypoxia was noticed in immature rats exposed to 6% CO_2 (Vannucci et al., 1995). Hemodynamics and blood-gas parameters were improved after dogs breathed a mixture of CO_2 and O_2 (Xie et al., 2005). Hypercapnia combined with hypoxia inhibited hypoxia-induced hematocrit increase, vascular remodeling and right ventricular hypotrophy, and protected against hypoxia-induced impairment of endothelial function (Ooi et al., 2000). Inducible nitric oxide synthase (iNOS) in serum of the plateau zokors increased significantly along with increase of CO_2 in their burrows in summer (our unpublished results). It is suggested that hypercapnia combined with hypoxia attenuates hypoxia-induced vasoconstriction of endothelial cell in blood vessels.

In conclusion, plateau zokors evolved unique physiological and biochemical adaptive mechanisms to obtain oxygen effectively from the hypoxic hypercapnic environment, and have strong tolerance to hypoxia and hypercapnia.

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