Short Communication

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Increase in O_2 Delivery with Hyperoxia Does Not Increase O_2 Uptake in Tetanically Contracting Dog Muscle

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Abstract: We investigated the influence of hyperoxia on O_2 uptake in tetanically contracting canine gastrocnemius. Hyperoxia showed neither increase in O_2 uptake nor decrease in lactate release, irrespective of increased O_2 supply, venous PO_2 and vascular resistance, as compared to normoxia, suggesting that hyperoxia decreases O_2 diffusion conductance and/or effective O_2 supply probably due to arteriovenous O_2 diffusion shunt. [Japanese Journal of Physiology, 50, 167–169, 2000]

Key words: diffusion shunt, oxygen consumption, lactate.

It is still uncertain that hyperoxia affects muscle oxygen consumption ($\dot{V}O_2$) during repetitive contractions [1]. There is both theoretical and experimental support for the idea that all precapillary O_2 losses, i.e., a longitudinal decrease in arteriolar oxygen tension (PO_2), an arteriovenous diffusion shunt, and diffusive exchange between arterioles and capillaries contribute significantly to limitations on O_2 extraction in the resting muscle [2]. Furthermore, O_2-diffusion shunt as an ineffective O_2 supply may affect $\dot{V}O_2$ in tetanically contracting muscle during hyperoxia.

We examined the influence of hyperoxia on $\dot{V}O_2$ and peripheral O_2 exchange during repetitive tetanic contractions with the canine gastrocnemius muscle group. Possible mechanisms for limiting $\dot{V}O_2$ by increasing PaO_2 have been discussed in relation to peripheral O_2 diffusion limitation for muscle $\dot{V}O_2$ [3–8] using both muscle venous effluent PO_2 (PvO_2), reflecting O_2 driving force of diffusion from erythrocyte to mitochondria, and $\dot{V}O_2/PvO_2$ ratio, reflecting O_2 diffusion conductance [9, 10].

Methods

Eight mongrel dogs (mean weight 13.2 ± 0.9 kg) were anesthetized with pentobarbital sodium (I.P., 30 mg/kg). The animals were ventilated by a respirator with room air except for hyperoxia. The left gastrocnemius-plantaris muscle group in the 8 dogs was surgically prepared using a method similar to that described by us previously [5, 6]. The right femoral artery and vein were exposed, and heparin ($1{,}000\ \mathrm{IU\,kg^{-1}}$) was administered intravenously. A thermostatically controlled infrared lamp was used to keep the surface of the muscle at 37°C. The isolated gastrocnemius was perfused by blood using methods described previously [6]. The perfusion pressure at the inlet of the arterial supply to the muscle was measured using a pressure transducer. Blood flow was measured using an electromagnetic flow meter (Nihon Kohden, Tokyo), the flow probe being set in the venous line.

The tendon was cut close to the calcaneus, clamped and connected to a force transducer (Showa model WBS-50 K, Tokyo). The length of the muscle was adjusted at 10 g force g^{-1} muscle weight. Isometric, tetanic contractions were induced by supramaximal stimuli (4 V, 0.2 ms duration) in trains of 200 ms duration. In each train, the frequency was 50 impulses/s. The frequency of trains was 1/s.

Each muscle took part in 3 min contraction bouts with 15 min intervals. The order of each bout was randomized in order to avoid the influence of successive 3 min contraction bouts. During hyperoxia, the dogs

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were ventilated with 100% O_2 in a Douglas bag.

Arterial and venous blood samples were simultaneously collected at 3 min of contraction time. All samples were measured for SO_2 with an OSM-2 (Radiometer, Copenhagen) and their pH, PCO_2 and PO_2 with a blood gas analyzer (Radiometer ABL 330, Copenhagen). $\dot{V}O_2$ was calculated from blood flow and arterio-venous O_2 concentration difference. The blood O_2 concentration in ml/dl (CO_2) was calculated from the relationship:

$$CO_2=[Hb]\times SO_2\times 1.34+0.0031\times PO_2,$$

where [Hb] is hemoglobin concentration in g/dl, SO_2 is fractional O_2 saturation, and PO_2 is in Torr. Hb concentration was measured by the cyanmethemoglobin method. The wet weight of muscle was 51±3 g. Lactate concentration was measured enzymatically (Lactate test, Boehringer, Mannheim).

All experimental data are presented as means±SE. A repeated measures ANOVA was used. Duncan's post hoc test was used to identify differences between two conditions (normoxia vs. hyperoxia) with significance being set at $p<0.05$.

Results and discussion

The main result of the present study is that an increase in O_2 delivery due to an increased CaO_2 by hyperoxia did not increase $\dot{V}O_2$ (Table 1). This result may be attributable to the peripheral diffusion limitation, diffusional shunt and/or vasoconstriction of the muscle due to high PaO_2.

The peripheral diffusion limitation as one of the limiting factors of $\dot{V}O_2$ is supported by our previous findings that high O_2-affinity erythrocytes decreased $\dot{V}O_2$ and PvO_2 in maximally contracting muscle at a constant O_2 delivery as compared with $\dot{V}O_2$ and PvO_2 of normal O_2-affinity erythrocytes [3, 7, 8]. The increase in muscle $\dot{V}O_2$ was closely related to the increase in PvO_2. However, the PvO_2 increased by hyperoxia did not augment the $\dot{V}O_2$ level as compared with normoxia, and the $\dot{V}O_2/PvO_2$ ratio during hyperoxia was decreased significantly (Table 1). This suggests that hyperoxia affects muscle $\dot{V}O_2$ through a mechanism other than O_2 diffusion limitation as manifested by the $\dot{V}O_2/PvO_2$ ratio [3–8].

Honig *et al.* [11] discussed that an arteriovenous diffusive O_2 shunt from arterioles of 40 μm or less in diameter could be very small because only the larger arterioles (>40 μm in diameter) are paired with venules, and separation distance between arterioles and venules is longer than 30 μm at rest and contraction. However, Tateishi *et al.* [12] observed a significant O_2 release from arterioles of 20 μm in diameter.

Table 1. O_2 supply and developed tension under normoxic and hyperoxic experimental conditions.

	Normoxia	Hyperoxia
pHa	7.36±0.01	7.36±0.01
PCO_2 (Torr)	40.1±1.1	40.1±1.0
PO_2 (Torr)	96.8±4.7	554.0±26.2*
Hb (g/dl)	15.3±0.6	15.2±0.6
CaO_2 (ml/dl)	19.9±0.9	22.1±0.9*
Lactate (mM)	1.6±0.1	1.8±0.1
Blood flow (ml min^{-1} 100 g^{-1})	91±8	90±8
Perfusion pressure (mmHg)	91±2	98±2*
Blood flow resistance (mmHg min 100 g ml^{-1})	1.05±0.10	1.15±0.09*
O_2 delivery (ml min^{-1} 100 g^{-1})	17.9±1.3	19.6±1.4*
$\dot{V}O_2$ (ml min^{-1} 100 g^{-1})	13.4±0.8	12.9±0.6
PvO_2 (Torr)	21.2±1.7	27.7±2.3*
$\dot{V}O_2/PvO_2$ ratio (ml min^{-1} 100 g^{-1} Torr^{-1})	0.67±0.08	0.50±0.07*
O_2 extraction (%)	75±3	67±4*
Initial tension (kg 100 g^{-1})	39.3±1.9	38.3±2.4
Tension at 3 min (kg 100 g^{-1})	22.7±1.5	22.7±1.5
Lactate release (μmol min^{-1} 100 g^{-1})	78±21	62±18

Values are means±SE; $n=8$ dogs. pHa, pH in arterial blood; PCO_2, partial pressure of CO_2 in arterial blood; PO_2, partial pressure of O_2 in arterial blood; Hb, hemoglobin concentration; CaO_2, arterial O_2 concentration of arterial blood; Lactate, lactate concentration in arterial blood; Blood flow resistance, perfusion pressure divided by blood flow; O_2 delivery, the product of arterial O_2 content and blood flow; $\dot{V}O_2$, O_2 consumption; PvO_2, partial pressure of O_2 in muscle venous effluent; O_2 extraction, arterio-venous O_2 content difference divided by arterial O_2 content; lactate release, the product of venous-arterial lactate concentration difference and blood flow. * Indicates statistically significant difference from corresponding value in normoxia ($p<0.05$).

Although we cannot suggest at this time whether longitudinal region contributes to O_2 diffusion shunt under the condition of hyperoxia, hyperoxia is assumed to increase the O_2 diffusion shunt due to the high driving force of arterial PO_2 in the arterio-venous counter-current interface [13].

If the constriction of resistance vessels induced by the high PO_2, as obtained in the present study (Table 1), leads to an altered distribution of blood flow [14], this may compromise the balance between regional O_2 demand and supply in contracting muscle under hyperoxia [15], probably resulting in a decrease in O_2-diffusion conductance secondary to a decrease in the surface area available for diffusion caused by the vasoconstriction. Indeed, the $\dot{V}O_2/PvO_2$ ratio decreased significantly (Table 1).

The present result seems to indicate that anaerobic metabolism occurred during tetanic contractions considering the increases in lactate release (Table 1) [16].

However, hyperoxia did not significantly decrease the lactate release. This might result from cancellation of the increase in O_2 delivery during hyperoxia by the increased O_2 diffusion shunt or the decreased $\dot{V}O_2/PvO_2$ ratio.

$\dot{V}O_2$ in the canine gastrocnemius did not increase by hyperoxia, although physically dissolved O_2 diffuses faster than hemoglobin binding O_2 [13] under the hyperoxic condition. This suggests that hyperoxia could decrease not only O_2 diffusion conductance ($\dot{V}O_2/PvO_2$ ratio) probably due to vasoconstriction, but also effective O_2 delivery probably due to shunting O_2 from arterioles to venules.

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