Is Hemoglobin Desaturation Related to Blood Viscosity in Athletes During Exercise?

Abstract

Several studies have suggested that athletes with low hemoglobin saturation during exercise may experience impaired pulmonary gas exchange during maximal exercise. Blood viscosity may be implicated in exercise-induced pulmonary hemorrhage in race horses. We hypothesized that blood rheology may contribute to impaired gas exchange and reduced hemoglobin saturation during exercise in humans. A group of 20 highly trained endurance athletes participated in this study, 9 with low hemoglobin saturation during exercise (Low-SpO2 group) and 11 with normal hemoglobin saturation (High-SpO2 group). All subjects performed a progressive exercise test conducted to VO2max. Venous blood was sampled at rest, 50% VO2max and maximal exercise. Blood viscosity (ηb) was measured at very high shear rate (1000 s⁻¹) and 37°C with a falling ball viscometer. The erythrocyte rigidity coefficient, “Tk”, was calculated using the Dittrich-Fass equation. At rest, no significant difference in ηb was observed between the two groups (3.00 ± 0.08 mPa·s vs. 3.01 ± 0.04 mPa·s for the Low-SpO2 and High-SpO2 group, respectively). At 50% VO2max and maximal exercise, ηb was higher in Low-SpO2 (p < 0.01). Tk decreased in High-SpO2 (p < 0.01) but remained unchanged in the other group during testing. The greater increase in ηb in the Low-SpO2 group during exercise may therefore have been due to the lack of reduction in Tk. As suggested by previous studies, the greater increase in blood viscosity in athletes with low hemoglobin saturation may lead to vascular shear stress. Whether this could impair the blood gas barrier and result in exercise-induced hypoxemia requires further study.

Key words

Hypoxemia · red blood cell · hemorheology · endurance

Introduction

Blood viscosity (ηb) is defined as the ratio of shear stress to shear rate. Shear rate is the velocity gradient between flowing layers of blood, whereas shear stress is the tangential force per unit area exerted on the vessel wall. In capillaries, i.e., at high shear rates, ηb is influenced by several hemorheological parameters: hematocrit (Hct), plasma viscosity (ηp) and red blood cell (RBC) rigidity [10]. Any increase in Hct, ηp or RBC rigidity leads to an augmentation in ηb. During both maximal and sub-maximal exercise [4,16], there are complex interactions between plasma viscosity, hematocrit and red blood cell rigidity [10], resulting in a significant increase in ηb.

Several studies have suggested that changes in blood rheology may be involved in both pulmonary capillary damage and gas exchange impairment observed in exercising animals and humans [1,3,20]. RBCs are implicated since adequate blood flow in capillaries for pulmonary gas exchange is primarily dependent on their deformability. Any increase in their rigidity and/or in ηb leads to a rise in vascular shear stress and to increased pulmonary vascular pressure [3,18,21]. In the case of exercise-induced pulmonary hemorrhage (EIPH) in thoroughbred horses, it has been suggested that the 2 to 5-fold increase in ηb, frequently observed during racing, may increase intra-capillary pressure and thus lead to capillary membrane damage [3,20]. However, McClay et al. [20] did not find significant differences in ηb and

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Bibliography

Hct level after exercise between bleeder and non-bleeder horses. In humans, it has been suggested that changes in nβ and/or RBC deformability might be involved in exercise-induced hypoxemia (EIH). EIH is defined as an inability to maintain an adequate level of oxygenation in arterial blood, leading to low partial pressure of oxygen and low hemoglobin saturation during intense exercise [8]. In master athletes with EIH, Aguillanu et al. [1] observed an upward shift in partial pressure of oxygen in arterial blood after six weeks of daily oral supplementation with polysaturated fatty acid, a diet known to increase RBC deformability and to decrease nβ [15]. Aguillanu et al. [1] did not perform hemorheological measurements, and it is still unknown whether nβ is higher or RBC deformability is lower in athletes with EIH. We hypothesized that the changes in RBC deformability during graded exercise would result in higher nβ in athletes with EIH. We thus studied hemorheological parameters in athletes with high or low hemoglobin saturation (SpO₂) levels during an incremental exercise test conducted to exhaustion.

Methods

Subjects

Twenty highly trained endurance athletes (triathletes and cyclists) participated in the study after giving informed written consent. All subjects were non-smokers with no history of lung or cardiac disease. All athletes were tested during an incremental exercise conducted to maximum oxygen uptake (VO₂max). When SpO₂ decreased more than 4% during at least the last three work rates (i.e., delta SpO₂: the difference between rest and peak exercise ≥4%), the athletes were assigned to the low SpO₂ group (Low-SpO₂, n = 8). The other athletes were assigned to the high-SpO₂ group (High-SpO₂, n = 11).

Protocol

The study protocol was approved by the local ethics committee. Athletes performed an incremental maximal exercise on a cyclo-ergometer conducted to VO₂max two hours after a standardized breakfast taken in the laboratory. Water intake was controlled for each subject before the test and no additional drink was allowed during exercise. Pulse oximetry SpO₂ was recorded at rest and during exercise. Before exercise, a catheter was inserted in the antecubital vein of the non-dominant arm. Venous blood samples were drawn at rest and during exercise for hemorheological parameters and plasma lactate measurements. The subjects were weighed before and after exercise.

Exercise test

Each subject performed the incremental maximal exercise test on a calibrated cyclo-ergometer (Ergoline type, Bitz, Germany). The test began with a 3-min warm-up at 60 W. Pedalling speed remained constant (70 rpm) throughout the test, and the load was increased by steps of 30 W every minute until VO₂max. Attaining two of three of the following criteria were used to determine the achieving of VO₂max: a respiratory exchange ratio value exceeding 1.10, a plateau in VO₂ with increased work rate, and attainment of age-predicted maximal heart rate (210 - [0.65 × age] ± 10%). A 5-min recovery period was then respected. VO₂, CO₂ output (VCO₂) and ventilation (V₆) were measured using a breath-by-breath automated exercise metabolic system (V₆max).

between weight loss and increase in hematocrit. Statistical significance was established at $\alpha = 0.05$.

**Results**

**Anthropometric and maximal cardio-respiratory characteristics**

Mean delta-SpO$_2$ (mean SpO$_2$ difference between rest and maximum exercise intensity) was 2.3 ± 0.2% for the High-SpO$_2$ group and 4.8 ± 0.3% for the Low-SpO$_2$ group. As shown in Table 1, both anthropometric data (age, weight, height) and maximal exercise response ($\text{VO}_{2\text{max}}$, $\text{V}_{\text{E}2\text{max}}$ and HR$_{\text{max}}$) were similar in the two groups. $\text{VO}_{2\text{max}}$ values show that the athletes were aerobically trained.

**Blood and plasma analysis**

At rest, $\eta_b$ (Fig. 1) was similar in the two groups and then increased significantly during exercise with higher values in the Low-SpO$_2$ group at 50% and 100% $\text{VO}_{2\text{max}}$. Hct (Fig. 2) and $n_p$ (Fig. 3) increased during exercise in a similar manner in the two groups. By contrast, the time course of Tk during exercise was different between the two groups (Fig. 4). In the High-SpO$_2$ group, Tk decreased between rest and 50% $\text{VO}_{2\text{max}}$ and between rest and $\text{VO}_{2\text{max}}$. No statistical change in Tk was observed in the Low-SpO$_2$ group with exercise. Plasma lactate concentrations were similar in the two groups, both at rest (2.2 ± 0.1 mM in the High-SpO$_2$ group and 2.0 ± 0.2 mM in the Low-SpO$_2$ group) and at $\text{VO}_{2\text{max}}$ (13.2 ± 0.4 mM in the High-SpO$_2$ group and 12.5 ± 0.3 mM in the Low-SpO$_2$ group).

**Weight loss**

Weight loss was 0.56 ± 0.03 kg for the High-SpO$_2$ group and 0.47 ± 0.05 kg for the Low-SpO$_2$ group. No statistical difference was found between the two groups. There was no significant correlation between weight loss and the increase in Hct between rest and $\text{VO}_{2\text{max}}$.

**Discussion**

The results show that blood viscosity increased significantly during incremental exercise in athletes, with a greater increase in the Low-SpO$_2$ group. The lack of improvement in red blood cell deformability observed in the Low-SpO$_2$ group during exercise may explain the higher increase of blood viscosity in this group and may have limited optimal gas exchange.

We used pulse oximetry, a non-invasive method, to assign the subjects to either the Low-SpO$_2$ or High-SpO$_2$ group. A minimum drop of 4% in SpO$_2$ for at least the last three steps of an incremental exercise test is required to conclude that the drop is significant [22]. In our study, SpO$_2$ for the Low-SpO$_2$ group ranged between 95% and 88%, indicating mild to moderate exercise-induced arterial hypoxemia as defined by Dempsey and Wagner [9].

It is well known that food intake modifies haemorheological parameters [7], i.e., a hyper-lipidic breakfast leads to a decrease in RBC deformability whereas a glucidic breakfast induces an increase.

**Table 1 Anthropic data and maximal cardio-respiratory characteristics for the two groups during incremental exercise testing**

<table>
<thead>
<tr>
<th></th>
<th>High-SpO$_2$ group (n = 11)</th>
<th>Low-SpO$_2$ group (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>22 ± 1</td>
<td>25 ± 2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72.5 ± 1.7</td>
<td>72.1 ± 2.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>181 ± 2</td>
<td>183 ± 2</td>
</tr>
<tr>
<td>$\text{VO}_{2\text{max}}$ (ml·min$^{-1}$·kg$^{-1}$)</td>
<td>63.8 ± 1.2</td>
<td>63.1 ± 2.0</td>
</tr>
<tr>
<td>$\text{V}_{\text{E}2\text{max}}$ (l·min$^{-1}$)</td>
<td>161 ± 6</td>
<td>163 ± 9</td>
</tr>
<tr>
<td>HR$_{\text{max}}$ (b·min$^{-1}$)</td>
<td>189 ± 3</td>
<td>186 ± 3</td>
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$\text{VO}_{2\text{max}}$, maximal O$_2$ uptake; $\text{V}_{\text{E}2\text{max}}$, maximal ventilation; HR$_{\text{max}}$, maximal heart rate.

**Fig. 1** Blood viscosity ($\eta_b$) at rest and during exercise in Low-SpO$_2$ group (□) and High-SpO$_2$ group (▲). §§ Significant difference between Low-SpO$_2$ and High-SpO$_2$ (p < 0.01); *** Significant difference between rest and 50% $\text{VO}_{2\text{max}}, 50\% \text{VO}_{2\text{max}}$ and $\text{VO}_{2\text{max}}$ (p < 0.001) in both groups.

**Fig. 2** Hematocrit (Hct) at rest and during exercise in Low-SpO$_2$ group (□) and High-SpO$_2$ group (▲). *** Significant difference between rest and 50% $\text{VO}_{2\text{max}}, 50\% \text{VO}_{2\text{max}}$ and $\text{VO}_{2\text{max}}$ (p < 0.001) in both groups.
crease. The breakfast was therefore controlled and met the standard usually used in clinical medicine before exercise [7]. Since drink intake before exercise also modifies blood rheology [27], water intake was carefully controlled in all subjects.

Blood viscosity has been assessed using the falling ball viscometer MT 90 Medicaest. It was demonstrated a few years earlier that it was a valid method to assess plasma viscosities and also blood viscosities in human [11,12]. Moreover, Doffin et al. [11] has demonstrated in a specific physical study that measurements of viscosities with the viscometer MT 90 are performed with a shear rate of 1000 s^{-1}. According to Dintenfass’s statement, it is absolutely possible to calculate Tk in our study because this author stated that the higher the shear rate is, the more specific for RBC deformability this index is [10]. Because measurements are performed at a high shear rate, it is also possible to hypothesize about the effects of blood rheology properties into small vessels like capillaries even if blood was drawn from antecubital vein. At high shear rates, \( \eta_b \) depends firstly on erythrocyte rigidity and secondly, on \( \eta_p \) and Hct whereas at low shear rates \( \eta_b \) depends firstly on aggregation properties instead of erythrocyte rigidity.

Resting hemorheological values found in this study for both groups are in accordance with data calculated in 20 healthy and middle sportsmen (26±1 yrs, 180±2 cm, 75.2±3.0 kg, \( \eta_b = 2.86\pm0.08\) mPa·s, \( \eta_p = 1.31\pm0.02\) mPa·s, Hct=41.3±1.0% and \( Tk = 0.63\pm0.02 \)). The range for Tk in this control group was 0.55–0.72 which indicates a great variability for this parameter in men without pathology.

As previously reported in sportsmen [4,16,30], our study showed that blood viscosity increased during exercise in both groups. But the greater increase of \( \eta_b \) in the Low-SpO₂ group was the more interesting result. Since we found both similar values and similar increases in Hct and \( \eta_p \) during exercise in both groups, RBC rigidity may be a key factor to explain the differences in \( \eta_b \) changes [10].

We found that RBCs became more deformable in the High-SpO₂ group during exercise whereas their basal deformability remained unchanged in the Low-SpO₂ group. At rest, there was a trend for the High-SpO₂ group to have higher values of Tk than Low-SpO₂ group, but there was no significant difference (\( p = 0.08 \)) and values were very narrow. These values were entirely within a non-pathological range of values as described by some studies at rest [4] and as described in our data measured in 20 healthy men (range 0.55–0.72). The drop in Tk could have partly compensated the rise in \( \eta_p \) and Hct during exercise, leading to lower \( \eta_b \) at \( V_{O_2} \text{max} \) in High-SpO₂. This result is interesting since it may reveal an adaptation restricted to only some endurance-trained athletes. Previous studies, mainly conducted in non-endurance trained athletes, have found an increase in Tk during maximal exercise [4,5]. It has been suggested that the increase in RBC rigidity during exercise may be related to increased plasma lactate concentration and pH decrease [5,19,25]. Indeed, when extra-erythrocyte lactate concentration increases, RBCs lose water by an osmotic process and become more rigid [19]. However, Hardeman et al. [16] observed a decrease in RBC rigidity despite increases in plasma lactate and acidosis during maximal exercise in endurance trained athletes. In the present study, the plasma lactate concentration was comparable in the two groups both at rest and maximal exercise. Changes in plasma lactate thus cannot explain the different time courses of Tk in the two groups.

Although our results showed a higher increase in \( \eta_b \) in athletes with Low-SpO₂, we did not find higher RBC rigidity in this group at maximal exercise. It thus seems that a complex interaction between RBC rigidity, Hct and plasma viscosity leads to whole blood viscosity changes.

Numerous factors may be responsible for Hct changes during exercise, including fluid shift, water loss and RBCs released from

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**Fig. 3** Time course of plasma viscosity (\( \eta_p \)) at rest and during exercise in Low-SpO₂ group (□) and High-SpO₂ group (▲). ***significant difference between rest and 50% \( V_{O_2} \text{max} \), 50% \( V_{O_2} \text{max} \) and \( V_{O_2} \text{max} \) only in High-SpO₂ group (\( p < 0.001 \)).

**Fig. 4** Time course of erythrocyte rigidity coefficient (Tk) at rest and during exercise in Low-SpO₂ group (□) and High-SpO₂ group (▲). ***significant difference between rest and 50% \( V_{O_2} \text{max} \), rest and \( V_{O_2} \text{max} \) only in High-SpO₂ group (\( p < 0.001 \)).

the spleen [26]. In the present study, we found no correlation between one indirect indicator of water loss by sudation, i.e., weight loss, and the increase in Hct. It has also been suggested that water trapping in muscle contributes to Hct changes [24]; however, we were unable to verify this hypothesis. Although less pronounced than in horses, the spleen may release stored erythrocytes into the bloodstream, leading to a rise in Hct. Isbister [17] showed that the increase in Hct was much lower in splenectomized subjects compared with healthy subjects during exercise.

The increase in np, frequently observed during exercise [14], is thought to be due to a rise in plasma protein content. Indeed, plasma concentrations of α1-globulins, α2-globulins, β-globulins and γ-globulins are augmented after moderate exercise [27].

We investigated blood viscosity and its components to clarify the possible relation to exercise-induced hemoglobin desaturation. Previous studies have shown reduced hypoxemia in master athletes receiving PUFA supplementation. RBC rigidity and/or increased blood viscosity may contribute to hypoxemia since 1) the rise in blood viscosity increases vascular shear stress at a high shear rate, i.e., in capillaries [3, 18, 21], and may be involved in the stress-failure of pulmonary capillaries [29]; and 2) the more deformable the RBCs, the more they can move in single file in pulmonary capillaries, leading to optimal gas exchange. McClay et al. [20] suggested that the hyperviscosity observed in thoroughbred horses during exercise could explain the higher prevalence of EIPH in these animals, although the pathogenesis of EIPH seems to be multi-factorial. In addition, Weiss et al. [28] reported that pentoxifylline, which is known to attenuate both vascular pressure and the severity of EIPH in horses, decreases RBC filtration pressure in blood by 26.6%. No studies have really shown in vivo, however, an effect of RBC rigidity and/or blood viscosity on pulmonary gas exchange, although animal studies have suggested it.

In summary, the results of this study indicate that athletes with reduced hemoglobin saturation during exercise also have a higher increase in np. RBC rigidity seems to be implicated in this difference in time course. The magnitude of the changes in blood viscosity during exercise in the Low-SpO2 group could impede blood flow and result in microvascular injury, as well as decreased tissue oxygenation. Although it is well known that blood rheology is involved in pulmonary blood flow distribution and the recruitment of diffusion capacity, further investigations are needed to more fully understand the relationship between hemorheology and exercise-induced hypoxemia.

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