THE TOTAL IONIC STATUS OF MUSCLE DURING INTENSE EXERCISE

G.J.F. Heigenhauser and M.I. Lindinger

Department of Medicine
McMaster University Medical Centre
Hamilton, Ontario
Canada L8N 3Z5

INTRODUCTION

During intense exercise, the high rate of glycolysis results in a large accumulation of intracellular lactate (La^-) and increased hydrogen ion concentration ([H^+]) (Spriet et al., 1985). High intracellular [H^+] during heavy exercise has often been implicated as a cause of muscle fatigue. A number of loci for fatigue have been suggested: excitation-contraction coupling (Fabiato and Fabiato, 1978), control of glycolytic flux at the level of phosphorylase (Chasiotis et al., 1983) and phosphofructokinase (Trivedi and Danforth, 1966) and impairment of ionic pumps and exchanges on the sarcoplasmic reticulum and sarcolemma (Nakamura and Schwartz, 1972).

To understand the factors influencing the [H^+] in the intracellular fluid, we need to identify changes in the independent variables associated with the ionic systems in this compartment (Stewart, 1981; 1983) in terms of physicochemical systems involving both dependent and independent variables and obeying two fundamental laws of physical chemistry - Electrical Neutrality and Conservation of Mass. The concentrations of the dependent variables such as bicarbonate ([HCO_3^-]), hydroxyl ion ([OH^-]), hydrogen ion ([H^+]), the ionized ([A^-]) and unionized ([HA]) weak electrolytes are dependent on three independent variables: the PCO_2, the total concentration of weak electrolytes ([Atot]), and the strong ion difference ([SID]). The [SID] is a term which describes the difference between the sum of the concentrations of weak basic cations ([Na^+]+[K^+]+[Mg^{++}]) and the strong acidic anions ([Cl^-]+[La^-]). The regulation of intracellular [H^+] of muscle during intense exercise depends on changes in the total ionic composition of both the intracellular and extracellular fluid. The purpose of the present paper is to describe the ionic changes that occur within the intracellular fluid of fast twitch, high glycolytic muscle during exhaustive exercise and the implications of ionic regulation on muscle fatigue.

METHODS

Twenty-one male Sprague-Dawley rats were used in the study. The animals were randomly assigned to two groups: resting non-exercise control group and an experimental exercise group. Three hours prior to the study,
TABLE I. Physico-chemical constants used in the calculation of the dependent ionic variables in muscle.

<table>
<thead>
<tr>
<th>Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K'_W$</td>
<td>$4.4 \times 10^{-14}$ Eq.1$^{-1}$</td>
</tr>
<tr>
<td>$K_C$</td>
<td>$2.34 \times 10^{-11}$ Eq.1$^{-1}$ mmHg$^{-1}$*</td>
</tr>
<tr>
<td>$K_3$</td>
<td>$6.0 \times 10^{-11}$ Eq.1$^{-1}$</td>
</tr>
<tr>
<td>$K_A$ (rest)</td>
<td>$5.5 \times 10^{-7}$ Eq.1$^{-1}$</td>
</tr>
<tr>
<td>$K_A$ (exercise)</td>
<td>$4.0 \times 10^{-7}$ Eq.1$^{-1}$</td>
</tr>
</tbody>
</table>

*Calculated from $K_C = K_x S_2$, where $K$, the apparent dissociation constant for CO$_2$, is $7.41 \times 10^{-1}$ Eq.1$^{-1}$; the CO$_2$ solubility coefficient is $0.0351$ Eq.1$^{-1}$ mmHg$^{-1}$ at 37°C and intracellular ionic strength.

The animals were injected via the tail vein with $^3$H mannitol and $^{14}$C-DMO for measurement of extracellular fluid volume and intracellular pH. The resting control group was killed by cervical dislocation. The exercise rats swam with an attached tail weight (5% of body mass) until they were unable to surface for 15s. The animals were removed from the water and killed by cervical dislocation. In both groups of animals, the abdomen was opened and 2 to 3 ml of blood were obtained in a heparinized syringe from the abdominal aorta. A sample of muscle (0.5g) was taken from the white gastrocnemius (WG). The muscle was immediately frozen and stored in liquid nitrogen until analyzed. The blood was analyzed for pH, PCO$_2$ and PO$_2$, ions (Na$^+$, K$^+$, Cl$^-$) and La$^+$ as previously described (Lindinger et al., 1986). Muscle total tissue water (TTW), intracellular and extracellular fluid volumes (ICFV and ECFV) were calculated from resting and exercised muscle (Lindinger and Heigenhauser, 1987). Intracellular ion concentrations were calculated from measurements of muscle ion contents measured by instrumental neutron activation analysis and muscle fluid volumes (Lindinger and Heigenhauser, 1987). Muscle pH was measured by a DMO technique. $[\text{Atot}]$ and its dissociation constant, $K_A$, were calculated from pH, $[\text{SID}]$ and $[\text{HCO}_3^-]$ obtained by titrating muscle homogenate samples with either CO$_2$ or NaOH and using the quantitative physico-chemical relationship described by Stewart (1981; 1983) (see Lindinger et al., 1987 for full description of methods). The dependent variables $[\text{H}^+]$, $[\text{OH}^-]$, $[\text{HCO}_3^-]$, $[\text{A}^-]$ and $[\text{HA}]$ for the whole muscle were calculated from the independent variables $([\text{SID}], [\text{Atot}]$ and PCO$_2$) measured from whole muscle and calculated using the equation 7A.1.2 from Stewart (1983):

\[
[H^+]^4 + [K_A + [\text{SID}]](H^+)^3 + \left(K_A ([\text{SID}] - [\text{Atot}]) - (K_C \times \text{PCO}_2 + K'_W)\right)(H^+) - \frac{K_A}{(K_C \times \text{PCO}_2 + K'_W) + K_3 \times K_C \times \text{PCO}_2} = 0
\]

The constants used in equation 1 are listed in Table I.

RESULTS

The duration of swimming of exercised rats was $4.4 \pm 0.5$ min. Compared to rest, at the end of exercise there was a 2.5% increase in TTW associated