Free Mg2+ concentration in the calf muscle of patients with glycogen phosphorylase and phosphofructokinase deficiency. A 31P MRS study in different metabolic conditions.

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Introduction

Skeletal muscles contain approximately 35% of total human body magnesium, which is an essential cofactor in a number of cell processes. Magnesium ions influence the equilibria of many reactions involved in cellular bioenergetics by interacting with phosphorylated molecules and interfere with the kinetics of ion transport across plasma membranes (1). There is considerable evidence that Mg^{2+} is actively transported and regulated, although the mechanisms are largely unknown (2). In the skeletal muscle variations of cytosolic pH, phosphocreatine (PCr) and inorganic phosphate (Pi) concentrations influence the complex multi-equilibrium system of the molecular species binding magnesium ions. As a consequence free cytosolic [Mg^{2+}] changes considerably in different metabolic conditions such as rest, exercise and recovery, showing an increase matched by a decrease of intracellular pH (3) during exercise and recovery.

To understand to which extent homeostasis of intracellular free Mg^{2+} is linked to pH, we assess by ^{31}P MRS the cytosolic pH and the free [Mg^{2+}] in the calf muscle in one patient with muscle phosphorylase deficiency (Mc Ardle disease), and two brothers both affected by phosphofructokinase deficiency (Tarui disease), in different metabolic conditions. In fact it is well known that both glycogenosis are characterized by lack of intracellular acidification during muscle exercise and recovery from exercise.

Methods

We studied 3 patients: a 42-year-old man affected by glycogen phosphorylase deficiency and two male brothers aged 18 and 10 years affected by a phosphofructokinase deficiency. Informed consent was obtained from each patient. We used a 1.5T General Electrics Medical Systems (Milwaukee, Wisconsin) Signa Horizon LX whole-body scanner. Subjects lay supine with a 6 cm diameter surface coil centred on the maximal circumference of the right calf muscle. Muscle aerobic exercise consisted of 1 minute of plantar flexion at incremental intensity. All patients were asked to perform an exercise to reach a PCr depletion of about 50% at the end of exercise. Spectra were acquired with a repetition time (TR) of 5 sec. Sixty-four FIDs at rest, and 12 FIDs during exercise for each level of work were averaged. During recovery 4-FID data blocks (20 sec) were recorded for 60 sec, while longer time blocks were collected thereafter. Spectra were post-processed by a time-domain fitting routine AMARES/MRUI (http://carbon.uab.es/mrui) and the free cytosolic [Mg^{2+}] and pH assessed from the chemical shift of β-ATP and Pi from PCr respectively (3).

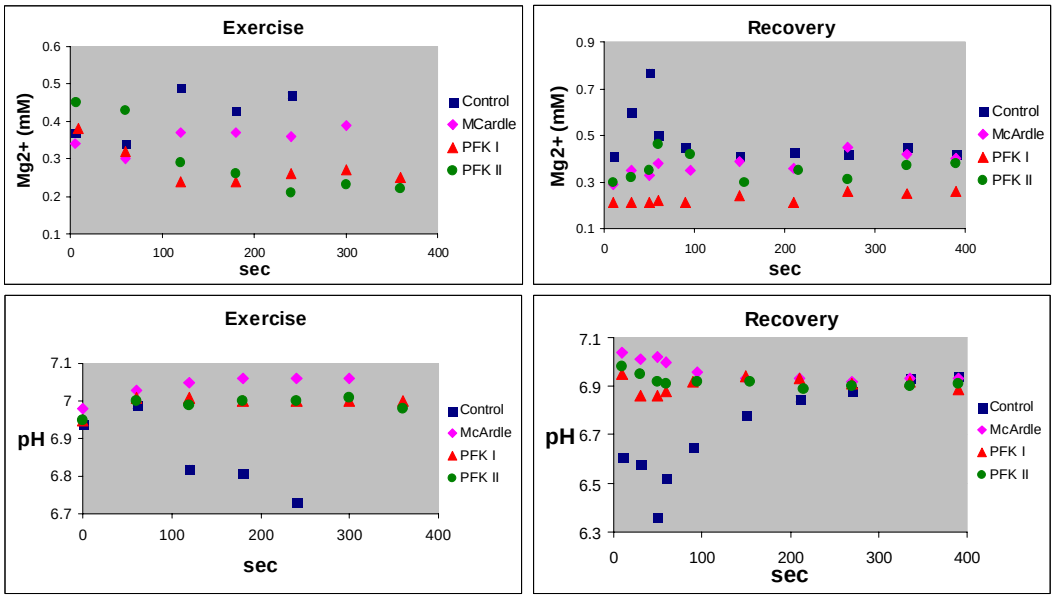

Figure. Patterns of cytosolic free magnesium concentration and pH at rest, during exercise and recovery in patients with different glycogenosis compared with a typical patterns from healthy volunteers with comparable PCr depletion. *Top left*: pattern of [Mg^{2+}] during exercise; *top right*: pattern of [Mg^{2+}] during recovery; *bottom left:* pH pattern during exercise; *bottom right:*

Results

As expected, all patients displayed a lack of intracellular acidosis during exercise. At rest only one PFK patient (PFK II) showed a free [Mg^{2+}] higher than the mean value found in 42 control subjects (0.45 mM; 0.32 $\pm$ 0.03 mM) (3). During exercise and recovery the McArdle patient did not show any significant change of free [Mg^{2+}], while both PFK patients showed decreased free [Mg^{2+}] during exercise. On the other hand, during recovery the pattern of free [Mg^{2+}] was different in the two PFK patients, with PFK II showing a moderate increase during early recovery.

Discussion

Our results show that: i) in the skeletal muscle homeostasis of free [Mg^{2+}] is strongly linked to pH as previously suggested by a study in healthy volunteers (3), and by computer simulation on a chemical model mimicking muscle cell cytosol (4); ii) the peculiar pattern of free [Mg^{2+}] during exercise in both PFK patients suggest that [Mg^{2+}] is influenced by the accumulation of the phosphorylated monosaccharides intermediates of glycogenolysis, an additional binding site for cytosolic Mg^{2+}, as shown by the accumulation of the phosphomonoesters peak in the ^{31}P MRS spectra of these patients.

References

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