In vivo assessment by 31P-MRS of skeletal muscle mitochondrial function in patients on long-term Home Parenteral Nutrition

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Introduction.

Phosphocreatine (PCr) is present in the skeletal muscle and other excitable tissues, where it represents a storage of readily available energy able to buffer sudden energy requirements of the cell. Typically, PCr is used during muscle contraction and is re-synthesised during recovery. When the metabolic stress is over, PCr is re-synthesised from ATP which in turn is synthesised by the energy-producing mitochondrial machinery. The rate of PCr re-synthesis during recovery from exercise assessed in vivo by phosphorus magnetic resonance spectroscopy (31P-MRS) is a reliable index of the functionality of muscle mitochondrial respiration in health and disease (1-3). We assessed the mitochondrial functionality in a group of patients affected by Chronic Intestinal Failure receiving long-term home parenteral nutrition (HPN) to understand whether and to what extent the nutritional status affects the bioenergetics of skeletal muscle.

Methods.

We studied 18 stable adult outpatients affected by Chronic Intestinal Failure (CIF) receiving long-term HPN (age 44 ± 16; 5 M, 9 F). Cause of CIF were: 10 Short Bowel, 7 Motility disorders, 1 Extensive mucosal disease. Duration of HPN was: 98 ± 74 months (range 7-238).

Informed consent was obtained from each patient. 31P-MRS was performed 8 hours after stopping HPN. The study 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 repetition of 1 minute 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. One hundred-twenty-eight FIDs at rest, and 12 FIDs during exercise for each level of work were averaged. During recovery 2-FID data blocks (10 sec) were recorded for 320 sec. Spectra were post-processed by a time-domain fitting routine AMARES/MRUI (http://carbon.uab.es/mrui). pH was assessed from the chemical shift of β-ATP and Pi from PCr respectively (4). The rate of PCr recovery was assessed by the time constant of the mono-exponential equation best -fitting the PCr recovery pattern. The control values were from a group of 50 healthy subjects (age 36 ± 15; 28 M, 22 F).

Result and Discussion.

Since the rate of PCr recovery is linked to the extent of cytosolic acidosis (2), being inversely correlated to the minimum pH value reached during recovery (pH min) (3), we assessed the mitochondrial functionality of patients reporting the time constants (TC) of the mono-exponential equation best-fitting the PCr recovery pattern as a function of pH min (figure 1).

Eleven patients showed a PCr recovery kinetics slower than controls. The group of patients with slow PCr recovery showed a higher [Pi] at rest ($P<0.05$), and faster rate of PCr depletion ($P<0.05$). In addition, the group of patients with slow PCr recovery did not show a statistically significant difference in the underlying disease, in the frequency of weekly HPN infusion, HPN duration , and HPN energy/day content, compared to the other 7 patients.

These results show that patients receiving long-term home parenteral nutrition may present an impairment in the skeletal muscle energy metabolism which, however is not related to the HPN infusion frequency, duration and energy content. Therefore, as protein calorie nutritional status did not differ between normal and impaired patients, we hypothesise that the mitochondrial dysfunction may be a consequence of the peroxidative stress due to intravenous lipid infusion leading to an increased concentration of reactive oxygen species (5), although the possibility of a deficiency of some essential nutrients playing a key role in mitochondrial metabolism cannot be discharged. However, the question why one third of patients did not develop any muscle impairment remains unanswered.

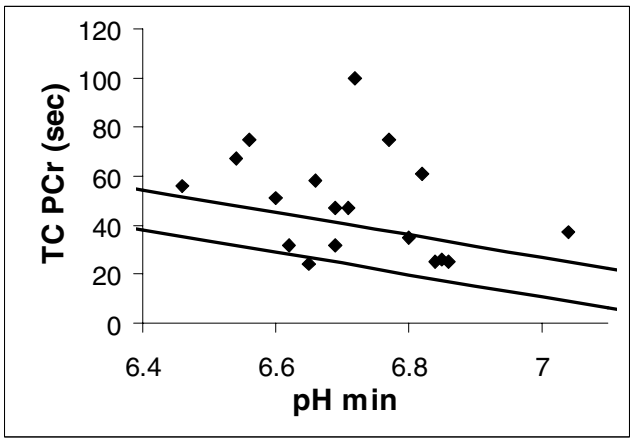

Figure 1. PCr recovery kinetics of patients reported as time constants (TC) as a function of pH min. The solid lines represent the 99% confidence bound around the regression line obtained in 50 control healthy subjects.

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