Bioenergetic Defects in Muscles of Polymyositis Patients: A Quantitative MRI and P-31 MRS Investigation

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Introduction

Polymyositis (PM) is an inflammatory muscle disease characterized by proximal weakness and severe fatigue, inflammation and/or fat infiltration in muscles, and elevated serum levels of muscle enzymes. Non-invasive MRI and P-31 magnetic resonance spectroscopy (P-31 MRS) have been used for evaluation of inflammatory myopathies (1-4). Cea et al., have described the initial metabolic defects in mitochondria of PM muscles in the lower leg, which showed minimal defects with MRI (3,4). In the present study, P-31 MRS was used to demonstrate the progression of disease in the more seriously affected proximal muscles of the thigh (4).

Methods

Nineteen PM patients and 11 normal subjects were examined with MRI to detect morphological abnormalities in the thigh muscles. P-31 MRS studies of the quadricep muscles were acquired during rest, graded levels of exercise, and recovery following exercise. Pi, PCr and ATP levels were determined from the resonance areas under the peaks. Concentrations of ADP, phosphorylation potential (PP), and work/energy cost ratios were calculated from the spectroscopic data as previously described (5). Data for PM patients and normal subjects were compared using the Student's 2-tailed t test.

Results

MRI of the thigh muscles in all patients showed significant inflammation and/or fat infiltration, which was verified by T1 and T2 relaxation times. During rest, PCr and ATP levels in PM muscles were 42% and 38% lower than that in normal muscles ($P < 0.0001$) (Figure 1). Pi/PCr ratios were 0.18 ± 0.01 and 0.13 ± 0.00 in the PM and control muscles ($P < 0.0001$), indicating a deficiency in PM muscles for generation and maintenance of ATP (Table 1). During exercise at 25% maximum voluntary contraction (MVC), PCr levels decreased, and the mean PCr concentration in the patient muscles was 45% lower than that in normal subjects ($P < 0.0001$). Pi/PCr ratio of exercising PM muscles rose to 0.46 and normal muscles to 0.32 ($P < 0.03$), again indicating a defect in oxidative phosphorylation in the patient group. The work/energy cost ratio (weight lifted / [Pi/PCr]) of PM patients was significantly lower than that of normal controls ($P < 0.0001$) because patients lifted less weight and the ratio increase was greater (Table 1). ATP levels, on the other hand, did not change significantly during rest, exercise or recovery, and mean ATP concentrations in PM muscles remained about 38% lower than that of normal muscles ($P < 0.0001$). ADP concentrations in the patients' muscles at rest were 4.3-fold higher than that in normal muscles, and 2.5-fold higher during exercise ($P < 0.0001$). The PP was 6.3 times lower in PM patients at rest and 2.9 times lower during exercise. (Table 1).

Discussion

In PM patients, the quadriceps muscles with severe MRI abnormalities showed significant decreases in ATP and PCr, which were concordant with weakness and fatigue. Elevated Pi/PCr ratios and ADP levels, along with decreased PP, indicated impaired mitochondrial oxidative phosphorylation. Cea, et al., showed that gastrocnemius-soleus muscles with minimal MRI abnormalities had normal levels of ATP and PCr, but substantial impairment in post-exercise P-31 MRS indices of oxidative metabolism. In addition, reduced proton efflux from muscle fibers indicated that an impaired blood supply was the primary factor for defective mitochondrial function (4). Recent EPI-DWI of PM muscles showed that the fractional volume of perfusion in the capillaries (f) was reduced in PM muscles (6). I**n summary,** MRI and P-31 MRS provided quantitative data for the evaluation of PM clinical status and the elucidation of pathophysiological mechanisms of disease progression.

References: 1. Park JH, et al., Radiology 1992; 185:322. 2. Newman ED and Kurland RJ, Arthritis Rheum 1992; 35:199-203. 3. Cea G, et al., Brain 2002; 125:1635-1645. 4. Reimers CD, et al., J Neurol 1994; 241:306-314. 5. Park JH, et al., Arthritis Rheum 1995; 38:68-77. 6. Qi J, et al., Radiology 2004; 233:1320.

Status	Subjects	Pi/PCr ratio	Work/energy cost	ADP µMoles	PP
Rest	CTL	0.13 ± 0.00		6.2 ± 0.8	377 ± 85
	PM	0.18 ± 0.01		26.5 ± 2.2	60 ± 5
	P value	<0.0001		<0.0001	0.004
25% MVC	CTL	0.32 ± 0.02	35.2 ± 3.2	15.7 ± 2.0	70 ± 14
	PM	0.46 ± 0.06	10.5 ± 1.2	40.0 ± 4.3	24 ± 3
	P value	0.03	<0.0001	<0.0001	0.008

Table 1. MRS data from rest and exercise.

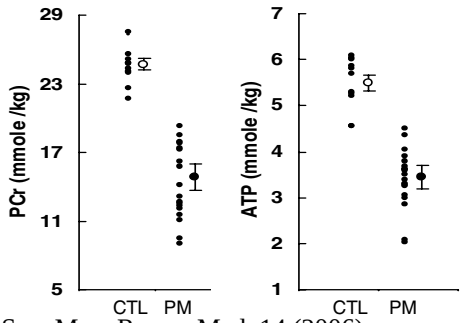

Figure 1. Individual PCr and ATP values at rest