Abnormalities in Magnesium (Mg) and ATP Levels Correlate with Muscle Dysfunction in Polymyositis

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INTRODUCTION: Polymyositis (PM) is an inflammatory muscle disease characterized by severe proximal weakness, fatigue, inflammation and/or progressive fat infiltration in the muscles. P-31 MRS has been used for characterization of PM muscles (1,2). Abnormalities such as decreased levels of ATP and PCr, the high energy phosphate compounds required for muscle contraction, and decreased PCr/Pi ratios have been quantitatively determined for evaluation of PM patients (1). Magnesium (Mg) is another important factor for muscle contraction because it is an essential cation for all reactions involving ATP, particularly those in the Krebs cycle, glycolysis, and creatine kinase, which are specifically related to ATP generation and maintenance. In a related imflammatory muscle disease, dermatomyositis (DM), Mg deficiencies have been demonstrated and shown to be correlated with muscle weakness (3). In this study, PM muscles were examined to detect abnormalities in Mg levels.

METHODS: Ten PM patients and 11 normal subjects were examined with P-31 MRS using a 1.5T magnet. Spectra of the quadricep muscles were obtained during each minute of a 6 minute rest period. For exercise, a weight equivalent to 25% MVC was secured on the ankle, and the subject raised his foot by contraction of the quadricep muscles once every five seconds for 6 minutes. The subject then repeated the exercise with a 50% MVC weight. The protocol was concluded with a 10 minute recovery period. ATP was quantitatively determined as previously described (4). ATP-bound Mg (MgATP) and free Mg were calculated from the MRS spectra according to the method of Gupta and Mottet (5,6).

RESULTS: During the initial rest period, enzymatically-active MgATP was 40% lower in the PM muscles as compared to normal values ($P < 0.0001$) (Table 1). There was no statistically significant differences between the free Mg levels in the PM and control muscles. With strenuous exercise at 50% MVC, there was no significant loss of MgATP in either group of subjects. However, during exercise, free Mg levels decreased by 15% in the PM muscles and increased in the control muscles. Thus, biologically-active free Mg in the diseased muscles was 42% lower than control values ($P < 0.006$). Total Mg values remained 40% lower in PM muscles ($P < 0.0001$).

DISCUSSION: Since Mg levels in serum do not accurately correlate with tissue levels, it is important to determine Mg in the quadricep muscles, which are severely affected in inflammatory myopathies. MgATP is the enzymatically-active form of ATP, and free Mg is a rate determining factor in the generation of ATP in the Krebs cycle. During exercise, MgATP and free Mg were markedly reduced in PM muscles. Thus, low levels of Mg may be related to weakness and fatigue observed in PM patients. In a preliminary trial with 5 myositis patients (4 PM and 1 DM), Mg and creatine were administered to determine whether this adjunct therapy could be improve muscle function. Levels of MgATP and PCr statistically increased with treatment and also correlated with improvements in muscle strength, work/ energy cost ratios, and health assessment questionnaires (7, 8).

In summary, low levels of MgATP and free Mg correlated with weakness and muscle dysfunction, thereby suggesting a role for Mg in the pathophysiology of PM. From our preliminary results with Mg and creatine therapy, a larger double-blind trial should be considered for patients with inflammatory myopathy.

Table 1. Mg levels in polymyositis and control subjects during rest and exercise. (Values expressed as mmol/kg muscle ±SEM)

SUBJECTS	STATUS	MgATP	β-ATP	%ATP free	Mg free	Mg total	% Mg free
Controls	REST	5.1 ± 0.1	5.5 ± 0.2	7 ± 1%	0.83 ± 0.09	5.9 ± 0.1	14 ± 2%
Polymyositis		3.1 ± 0.3	3.3 ± 0.3	8 ± 1%	0.66 ± 0.08	3.7 ± 0.4	18 ± 2%
P value		< 0.0001	<0.0001	NS	NS	0.0002	NS
Control	50% MVC	5.0 ± 0.2	5.3 ± 0.2	6 ± 1%	0.96 ± 0.12	5.9 ± 0.2	16 ± 2%
Polymyositis		3.0 ± 0.2	3.3 ± 0.3	9 ± 0%	0.56 ± 0.04	3.6 ± 0.3	16 ± 2%
P value		< 0.0001	< 0.0001	0.0008	0.006	< 0.0001	NS

References: 1. Qi J, et al. ISMRM 2006; 14:1683. 2. Cea G, et al. Brain 2002; 125:1635-45. 3. Niermann K, et al. Arthritis Rheum 2002;46:475-88. 4. Park JH, et al. Arthritis Rheum 1995; 38:68-77. 5. Gupta RK, et al. J Biol Chem 1978; 253: 6172-76. 6. Mottet I, MAGMA 1994; 2:101-107. 7. Qi J., et al. Radiology (RSNA abst.) 2005; 400. 8. Park JH, et al. Arthritis Rheum 2005; 52:S316.