Clinical Use of ^{31}P -Nuclear Magnetic Resonance Spectroscopy for Muscle Damage in Uremia

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Dear Sir,

It is generally known that uremic patients often complain of fatigue and muscle weakness [1]. Recently, nuclear magnetic resonance (NMR) spectroscopy with ^{31}P has enabled the non-invasive evaluation of muscle energy metabolism [2]. Using this new method, we evaluated the muscle energy metabolism in uremia without biopsy. Twenty-three uremic patients, 15 non-dialyzed uremic patients due to chronic glomerulonephritis (CRF_{cg}; Cr 8.07 ± 2.54 mg/dl) and diabetes mellitus (CRF_{DM}; Cr 7.88 ± 1.64) and 8 dialyzed uremic patients (HD; Cr 14.7 ± 4.62), and 6 control subjects (Cr 1.10 ± 0.02) were examined. NMR studies were conducted with a 1.5 tesla whole body magnet interfaced with Magnetom (Siemens, Germany) operating at 25.74 MHz for phosphorus, using a surface coil 8 cm in diameter with 3 turns. The ^{31}P -NMR spectrum was accumulated with 32 signals using a single pulse sequence (10-second interpulse interval). Figure 1 shows the typical ^{31}P -NMR spectra obtained from musculus biceps femoris in uremia. Signals are observed from inorganic phosphate (Pi), phospho-creatine (PCr), adenosine triphosphate (ATP; γ -, α -, β -) in all muscles. The relative concentrations of ATP, PCr and Pi in skeletal muscle were measured by integration of signal areas, assuming that normal human muscle contains 5.5 mM ATP/kg wet weight [3]. The intracellular pH (pHi) was calculated from the chemical shift difference (σ) between PCr and Pi signals: $\text{pH} = 6.75 + (\sigma - 3.27) / (5.69 - \sigma)$ [4].

Fig. 1. Representative spectra obtained from uremic muscle. The Pi, PCr and ATP (γ -, α -, β -) signals are identified in all subjects.

The mean relative concentrations of metabolites containing phosphate and pHi in muscle are shown in figure 2. Uremic muscles had significantly lower ATP, PCr and higher Pi concentrations than that of non-uremia. However, there was no significant difference in pHi between non-uremic and uremic muscles, even with extracellular acidosis. Oxidative phosphorylation and glycolysis are impaired in uremic patients and consequently these

impairments reduced the ability to produce ATP and PCr in uremic muscle [5]. The reason why intact intramuscular pH in uremia measured by ³¹P-NMR was not acidotic is probably as follows. In the case that extracellular acidosis developed gradually, intramuscular pH may not be affected or other elements may have

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mM/kg wet wt 25H

Control (n= 6) CRF(CGN) (rv 10) [WS] CRF(DM) (π=5) HD (n= 8)

7.04

7.02

-7.00

I

α

6.98

6.96

Fig. 2. The mean relative concentrations of metabolites containing phosphate and intramuscular pH. *p < 0.05 vs. control.

affected the chemical shift of Pi [6]. We suggest that ³¹P-NMR spectroscopy is a convenient and useful non-invasive examination for the evaluation of muscle damage in uremia, especially uremic myopathy, without biopsy, and the lower concentrations of ATP and PCr in skeletal muscle may be attributable to the easy fatigability and muscle weakness associated with uremia. Gadian DG, Radda GK, Dawson MJ, et al: pH measurements of cardiac and skeletal muscle using ³¹P NMR; in Intracellular pH: Its Measurement, Regulation and Utilization in Cellular Functions. New York, Liss, 1982, pp 61–77.

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