Myocardial magnesium depletion during cyclosporine treatment, associated with reciprocal calcium overload, can be prevented by plentiful dietary magnesium supply

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Recently Millane et al. [3] reported serial measurements of myocardial magnesium in heart transplant patients receiving cyclosporine; they found hypomagnesemia in all patients and a prevalence of 60% of myocardial magnesium depletion. Since dietary magnesium deficiency is known to increase myocardial calcium levels in experimental animals [1], similar effects might occur in cyclosporine-treated patients. This experimental study was carried out to obtain additional information about the influence of cyclosporine on intracellular electrolyte distribution.

In adult male Sprague-Dawley rats serum and tissue magnesium and calcium concentrations were determined by atomic absorption spectrometry [2] after 3 months of cyclosporine treatment (20 mg/kg daily); olive oil was administered to control animals. Rats were kept on three different diets with low (100 ppm magnesium, corresponding to 25% of their requirement), standard (1000 ppm), or plentiful (10 000 ppm) magnesium levels (magnesium-L-aspartate hydrochloride; Verla Pharm, Germany). Statistical evaluation was performed by analysis of variance.

The results are shown in Table 1. In control animals myocardial magnesium and calcium concentrations were not influenced by the different diets. Bone magnesium, representing the main magnesium store, clearly reflected magnesium intake and decreased when cyclosporine was given (data not shown) in animals under low or and standard chow. Correspondingly, serum magnesium concentrations decreased significantly ($P < 0.05$). Myocardial magnesium concentrations decreased as well, and myocardial calcium concentrations clearly increased. These electrolyte shifts were completely prevented by plentiful magnesium supply.

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Recently we have shown that cyclosporine decreases not only serum magnesium but also magnesium concentration of the femur bone and the kidney [4]. A reduction in tissue magnesium concentration by cyclosporine may negatively influence its physiological function as has been shown in the kidney. In accord with Millane et al. [3], our results confirm that the myocardial magnesium concentration decreases and its calcium concentration increases due to cyclosporine treatment under standard and reduced magnesium intake. Millane et al. [3] therefore expected accelerated coronary artery disease and myocardial fibrosis as long-term clinical effects. If this is true, plentiful magnesium supply may protect against morphological and functional alterations due to cyclosporine-induced magnesium depletion.

References

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Table 1. Electrolyte concentrations in serum and myocardium in cyclosporine-treated and control rats under different levels of magnesium intake

Diet and treatment	Serum magnesium (mmol/l)	Myocardial magnesium (mmol/kg dm)	Myocardial calcium (mmol/kg dm)
100 ppm			
Control (n=9)	0.63 ± 0.1	36.8 ± 0.6	4.7 ± 0.1
Cyclosporine (n=12)	0.35 ± 0.007	32.7 ± 0.1	12.8 ± 3.0
1000 ppm			
Control (n=10)	1.25 ± 0.14	37.5 ± 0.11	4.5 ± 0.6
Cyclosporine (n=6)	0.75 ± 0.2	35.4 ± 2.6	9.1 ± 3.1
10000 ppm			
Control (n=12)	1.52 ± 0.16	37.6 ± 0.6	4.2 ± 0.3
Cyclosporine (n=11)	1.87 ± 0.38	38.0 ± 1.2	4.7 ± 0.2

dm, Dry matter