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Loss of Cardiac Magnesium in Experimental Heart Failure Prolongs and Destabilizes Repolarization in Dogs.

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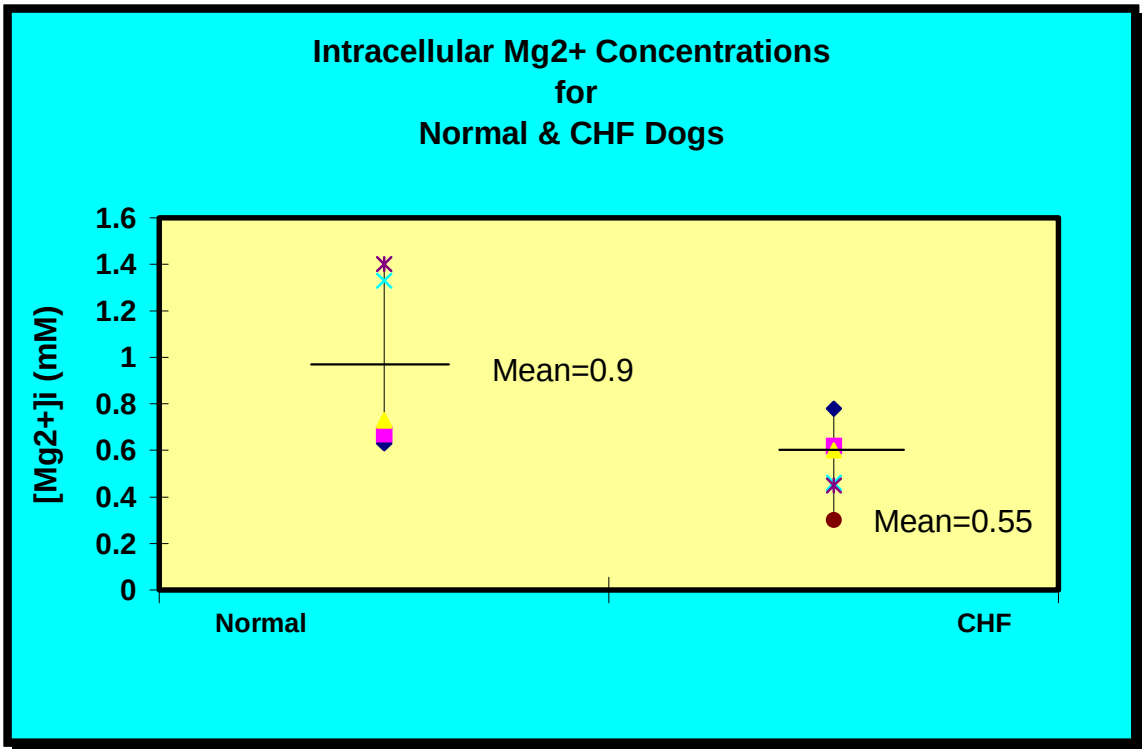
OBJECTIVES: We sought to determine whether heart failure results in loss of cardiac magnesium sufficient to alter cellular electrophysiology.

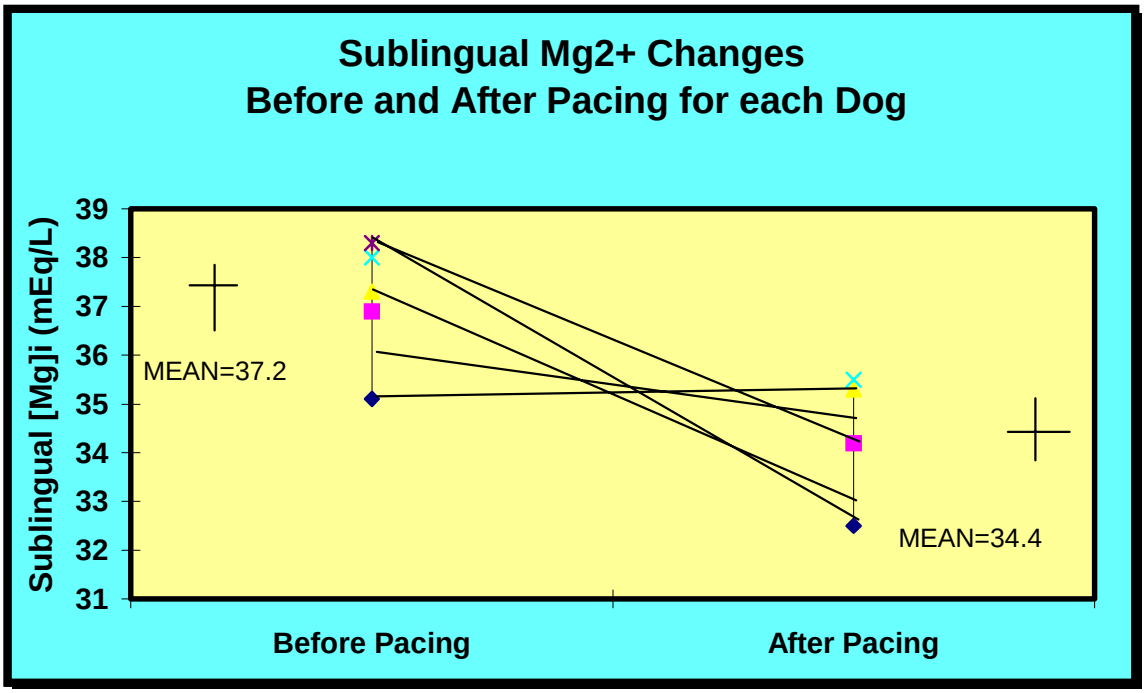
BACKGROUND: Free magnesium has numerous intracellular roles affecting metabolism, excitability and RNA synthesis. Total cardiac magnesium content is reduced in heart failure, but it is unclear whether magnesium loss is primary or iatrogenic. Furthermore, it is unknown whether free magnesium levels are affected or whether a change in free magnesium would alter cellular electrophysiology.

METHODS: Eight mongrel dogs underwent demand ventricular pacing (VVI) at 250 beats/min for 3 weeks to induce heart failure. Sublingual epithelial magnesium was measured before pacing and at death. (Exatest, IntraCellular Diagnostics) Left ventricular myocytes were isolated and loaded with Mag-Indo-1 to measure free magnesium ([Mg2+]i); myocytes from eight normal dogs served as controls. To test whether changes in [Mg2+]i in this range could alter cellular repolarization, current-clamped myocytes were dialyzed with 0.5 or 1.0 mmol/liter MgCl2.

RESULTS: Mean sublingual epithelial magnesium fell significantly in the paced animals, from 36.9 +/- 0.5 to 33.9 +/- 0.7 mEq/liter ($p < 0.01$). Mean cardiac [Mg2+]i was significantly lower in the dogs with heart failure--0.49 +/- 0.06 versus 1.06 +/- 0.15 mmol/liter ($p < 0.003$). Time to 90% repolarization was significantly shorter in cells dialyzed with 1.0 mmol/liter compared with 0.5 mmol/liter MgCl2 in myocytes from normal dogs or dogs with heart failure (596 +/- 34 vs. 760 +/- 58 ms in normal dogs and 586 +/- 29 vs. 838 +/- 98 ms in dogs with heart failure; $p < 0.05$ for each).

CONCLUSIONS: Experimental heart failure results in both tissue and cardiac magnesium loss in the absence of drug therapy. Free cardiac magnesium is significantly reduced, possibly contributing to abnormal repolarization in heart failure.


Intracellular Mg2+ Concentrations
for
Normal & CHF Dogs
[Mg2+]i (mM)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Mean=0.9
Mean=0.55
Normal
CHF


Sublingual Mg2+ Changes
Before and After Pacing for each Dog
Sublingual [Mg]i (mEq/L)
39
38
37
36
35
34
33
32
31
MEAN=37.2
MEAN=34.4
Before Pacing
After Pacing