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THE EMERGING ROLE OF VITAMIN D3 IN PROTECTING ISCHEMIC TISSUES

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Shih and colleagues present their findings regarding pretreatment with intravenous Vitamin D3 in a bilateral rat hindlimb ischemia/reperfusion model (1). In this study, bilateral femoral arteries were occluded for 3 hours, followed by 3 hours of reperfusion, which was selected based on prior studies (2). The intravenous dose was chosen appropriately, based on prior studies. Lung tissue and tibialis anterior muscle from each leg were harvested for wet/dry weight ratio and microscopic analysis. Blood was analyzed to determine blood urea nitrogen (BUN), creatinine (Cr), liver transaminases, interleukin (IL)-6, tumor necrosis factor- α (TNF- α) and heme oxygenase-1 (HO-1) levels. Preischemic treatment with vitamin D3 reduced muscle and lung edema, which was associated with a reduction in serum IL-6 levels. No differences were detected in serum TNF- α , BUN, Cr or liver transaminases.

These data support accumulating early evidence that vitamin D3 may be able to protect ischemic tissues (3,4). Patients awaiting elective surgery requiring an element of ischemia-reperfusion could potentially be protected from reperfusion injury by a preoperative vitamin D3 regimen. Also, one might envision a situation in which chronic vitamin D3 supplementation could reduce morbidity and mortality attributable to cardiovascular disease, the leading cause of death in the United States (5). Although these are interesting possibilities, more animal studies need to be performed. Whether vitamin D3 can protect the heart and brain from ischemic injury has not been determined, but seems promising. The protective mechanisms also need to be defined; it is unclear whether the observed benefit is due to modulation of calcium metabolism or effects on other pathways.

As with any study, this manuscript does have some limitations. The bilateral hindlimb ischemia model is not an ideal model of peripheral vascular disease. Certainly bilateral lower extremity ischemia can occur secondary to aortoiliac occlusive disease, but in clinical practice the more common situation is acute unilateral lower extremity ischemia. Use of a unilateral hindlimb ischemia model also would have permitted direct comparison of injured muscle to the unaffected contralateral limb. Also, the authors assessed remote lung injury as a consequence of hindlimb ischemia, but pulmonary inflammatory complications following limb reperfusion

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are not a relevant clinical entity. Additionally, it would be helpful to perform further analysis of molecular pathways to begin to determine the mechanism of action of vitamin D3. Despite its minor limitations, this manuscript by Shih and colleagues has certainly advanced our understanding of the emerging role of vitamin D3 in ischemic tissue protection.

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