The effects of a NAD(P)H oxidase inhibition on matrix metalloproteinases and TIMP-1 in the *mdx* diaphragm

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Int J Exerc Sci 2(1): S36, 2009. Duchenne muscular dystrophy (DMD) is characterized by devastating muscle degeneration that includes oxidative stress, loss of contractile tissue, muscle weakness and increased fibrosis in respiratory muscles (e.g., diaphragm). The *mdx* mice diaphragm undergoes a progressive degeneration similar to that occurring in patients with DMD. We showed that apocynin, a NAD(P)H oxidase inhibitor, protects against reduction in diaphragm mass, oxidative capacity, and apoptosis. We hypothesized that apocynin (1.5mmol/L per day) would attenuate extramyocyte space and collagen content by ameliorating matrix metalloproteinases (e.g., MMP-2, MMP-9), tissue inhibitors of metalloproteinases (e.g., TIMP-1) and transforming growth factor-β (TGF-β) in the *mdx* diaphragm. Eight to nine week old *mdx* mice and age-matched C57BL wild-types were divided into 4 groups: wild-type controls + water (WW, n=7); wild-type controls + apocynin (WA, n=7); *mdx* mice + water (MW, n=7), and *mdx* mice + apocynin (MA, n=7). After 8 days of treatment, the diaphragm was extracted. Both MMP-2 (-22.6%) and MMP-9 (-27.8%) were lower in MW than WW. TIMP-1 (+61.3 %) and TGF-beta levels (+39.4%) were higher in MW than WW. MMP-2 (-21.8%) and TIMP-1 (-8.5%) levels were significantly decreased with apocynin in the *mdx* diaphragm. Our findings indicate cell protection of apocynin against fibrosis in the *mdx* diaphragm by regulating the protein levels of MMP-2/9 and TIMP-1. Supported by a grant from NIH (AR054084) & J.L. Huffines Institute in Texas A&M University