Nifedipine treatment reduces resting calcium concentration, oxidative and apoptotic gene expression, and improves muscle function in dystrophic mdx mice

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Duchenne Muscular Dystrophy (DMD) is a recessive X-linked genetic disease, caused by mutations in the gene encoding dystrophin. DMD is characterized in humans and in mdx mice by a severe and progressive destruction of muscle fibers, inflammation, oxidative/nitrosative stress, and cell death. In mdx muscle fibers, we have shown that basal ATP release is increased and that extracellular ATP stimulation is pro-apoptotic. In normal fibers, depolarization-induced ATP release is blocked by nifedipine, leading us to study the potential therapeutic effect of nifedipine in mdx muscles and its relation with extracellular ATP signaling. Acute exposure to nifedipine (10 ?M) decreased [Ca 2+]r, NF-?B activity and iNOS expression in mdx myotubes. In addition, 6-week-old mdx mice were treated with daily intraperitoneal injections of nifedipine, 1 mg/Kg for 1 week. This treatment lowered the [Ca2+]r measured in vivo in the mdx vastus lateralis. We demonstrated that extracellular ATP levels were higher