Do antioxidants inhibit oxidative-stress-induced autophagy of tenofibroblasts?

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Abstract

Recent research on tendinopathy has focused on its relationship to programmed cell death. Increased autophagy has been observed in ruptured rotator cuff tendon tissues, suggesting a causal relationship. We investigated whether autophagy occurs in human rotator cuff tenofibroblast death induced by oxidative stress and whether antioxidants protect against autophagic cell death. We used H2 O2 (0.75 mM) as oxidative stressor, cyanidin (100 µg/ml) as antioxidant, zVAD (20 µM) as apoptosis inhibitor, and 3-MA (10 mM) as autophagy inhibitor. We evaluated cell viability and known autophagic markers: LC3-II expression, GFP-LC3 puncta formation, autolysosomes, and Atg5-12 and Beclin 1 expression. H2 O2 exposure increased the rates of cell death, LC3-II expression, GFP-LC3 puncta formation, and autolysosomes. After we induced apoptosis arrest using zVAD, H2 O2 exposure still induced cell death, LC3-II expression, and GFP-LC3 puncta formation. H2 O2 exposure also increased Atg5-12 and Beclin 1 expressions, indicating autophagic cell death. However, cyanidin treatment reduced H2 O2-induced cell death, LC3-II expression, GFP-LC3 puncta formation, and autolysosomes. Cyanidin and 3-MA similarly reduced the cell-death rate, and Atg5-12 and Beclin 1 expression. This study demonstrated that H2 O2, an oxidative stressor, induces autophagic cell death in rotator cuff tenofibroblasts, and that cyanidin, a natural antioxidant, inhibits autophagic cell death.