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HEMODIALYSIS (HD) INDUCES INTERLEUKIN-6 EXPRESSION, APOPTOSIS AND PROTEOLYSIS IN THE SKELETAL MUSCLE

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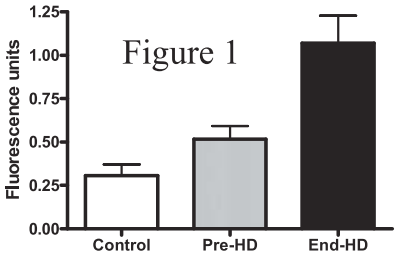
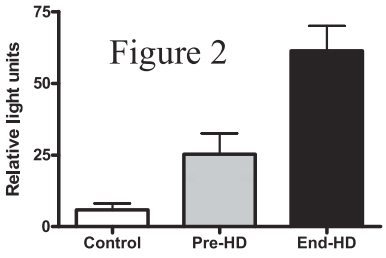
Muscle atrophy results from augmented proteolysis and accelerated apoptosis. We hypothesized that muscle wasting in HD patients (pts) is due to activation of apoptotic and proteolytic cascades during HD and measured the caspase-3 activity, apoptosis, abundance of 14 kD actin fragments, ubiquitinized actin fragments and interleukin-6 (IL-6) expression in the skeletal muscle of 8 HD pts and 6 healthy volunteers. Muscle protein kinetics was studied using primed constant infusion of L-(ring $^{13}C_6$) Phenylalanine. The content of IL-6 (pg/ml) measured in the soluble fraction of the muscle was higher pre-HD (7.74±2.86) compared to controls (0.62±0.20) ($p<0.05$), which increased further at end- HD (347.01±74.0 $p<0.001$)





Apoptosis was significantly higher at pre-HD and end-HD compared to controls, (Figure1), but increased muscle proteolysis was observed only at end-HD. Increase in caspase-3 activity at end-HD was associated with augmented apoptosis and also increased abundance of 14 kD actin fragment. The content of ubiquitinized actin fragment increased at end-HD indicating that the actin is being targeted for proteolysis (figure2). Thus, HD activates caspase-3 and ubiquitin proteasome cascade resulting in apoptosis and proteolysis. The muscle protein catabolism was strongly associated with caspase-3 activity in controls but in ESRD patients caspase-3 and muscle IL-6 content were the co-determinants. Thus activation of apoptosis and proteolysis by IL-6 mediate muscle wasting in ESRD.