An experimental analysis of the occurrence, progression, and pathological mechanisms associated with Achilles tendinopathy induced by hyperuricemia

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Introduction: Hyperuricemia (HUA) is a common metabolic disease with an increasing incidence that can negatively affect multiple tissues and organs. Elevated serum uric acid levels can lead to uric acid crystal formation, trigger gout, and may cause Achilles tendinopathy and Achilles tendon rupture. However, there is limited research on hyperuricemia-related Achilles tendinopathy. This study aims to establish a rat model of chronic hyperuricemia and explore its effects on Achilles tendon tissue and its potential pathological mechanisms.

Method: This study divided 80 male SD rats into 40 in the control group and 40 in the HUA group.（Male rats exhibit more stable hormone levels in chronic diseases） The HUA group received a daily gavage of potassium oxonate (750 mg/kg) and adenine (100 mg/kg) to induce hyperuricemia, while the control group was given 0.5% sodium hydroxypropyl cellulose. Bilateral Achilles tendon specimens were collected at 4, 6, and 10 weeks, along with blood samples to measure serum uric acid levels. The samples underwent analysis for uric acid content, biomechanical properties, histological characteristics and transmission electron microscopy (TEM) evaluation.

Result: The serum uric acid levels in rats within the HUA group significantly increased to 94.85 ± 31.37 μmol/L three weeks after modeling, compared to 28.33 ± 14.00 μmol/L in the control group. With no notable fluctuations observed between 6 to 10 weeks. Uric acid accumulation in the Achilles tendon tissue rose to 24.24 ± 10.75 μmol/L at four weeks. It stabilized at 64.78 ± 10.75 μmol/L by six weeks, indicating a correlation between serum uric acid levels and tendon uric acid content. The ultimate tensile strength assessments revealed a decline in the failure force for the HUA group, with values decreasing from 59.35 ± 4.76 N after 4 weeks to 62.38 ± 6.63 N after 6 weeks, representing a total reduction of 29%.Histological examination indicated collagen fiber degeneration beginning at four weeks and becoming more pronounced by ten weeks. Gomori staining showed uric acid crystals appearing at six weeks, with significant deposition by ten weeks. Increased cell apoptosis was observed in the tendons of the HUA group. Immunofluorescence analysis of TUNEL indicated that the expression of cell apoptosis in the HUA group was significantly increased. In the HUA group, TEM revealed that the collagen fibers within the HUA group exhibited a reduction in both thickness and quantity. Furthermore, there was a significant decrease in mitochondria and a marked reduction in the cristae within each mitochondrion. These findings indicate notable degeneration and structural damage to the mitochondria. Reflecting worsening tendon inflammation and collagen matrix degeneration.

Discussion: Long-term hyperuricemia enters the acute phase at around 6 weeks, with uric acid crystal deposition occurring at around 10 weeks. However, even before uric acid crystal deposition, the resulting inflammation has already begun to affect the physiological functions of the tissue, and this effect may be related to mitochondrial damage.

Significance/Clinical Relevance: Chronic hyperuricemia leads to uric acid buildup in tendons, causing inflammation and damaging tendon cell mitochondria. This results in increased cell death, collagen degeneration, tendinopathy, and weakened tendon mechanics. As a systemic metabolic disorder, hyperuricemia can also harm other musculoskeletal tissues. Thus, early preventive measures and interventions are crucial in clinical practice.