Inflammatory Cytokines in the Painful Ankle Joint: Arthritis and Osteochondral Lesions

Foot & Ankle Category: Ankle Arthritis

Author(s):
Kenneth J. Hunt, MD
Ariel Palanca, MD
Roberto Valladares,
Loretta B. Chou, MD

Introduction
The presence of inflammatory cytokines in synovial fluid has been associated with painful and degenerative conditions in joints, including the knee and cervical and lumbar spine. However, the role of cytokines in painful ankle conditions has not yet been investigated. Our goal is to determine whether inflammatory cytokines are higher in painful ankles with osteoarthritis compared to those with osteochondral lesions of the talus (OLTs). We hypothesize that greater concentrations of inflammatory cytokines will be present in ankle arthritis but not in OLTS.

Methods
We enrolled consecutive patients undergoing surgical treatment for ankle arthritis or OLT. Synovial fluid was obtained from each ankle using a lavage technique at the beginning of the planned surgical procedure. Samples were also obtained from asymptomatic control ankles as well. Pre-operative visual analog pain scale (VAS) and AOFAS ankle scores, Kellgren Lawrence scores, Outerbridge scores, size and depth of osteochondral defects, and follow-up VAS and AOFAS ankle scores were collected. Ankle lavage samples were assessed for levels of tumor necrosis factor (TNF-alpha), matrix metalloproteinases (MMP-1, MMP-3, and MMP-9), interleukins (IL-1 and IL-6), and macrophage inflammatory protein 1 (MIP-1), Statistical analysis was performed by the Mann-Whitney t test and multiple group comparisons was performed using ANOVA and post-hoc analysis. Pearson correlations were calculated comparing cytokine levels with clinical and radiographic variables.

Results
There were 46 patients total: 22 with OLTS, 15 with ankle arthritis, and 9 controls. Compared to control and OLT specimens, specimens from ankles with osteoarthritis had significantly greater concentrations of MMP-1, MMP-3, MIP-1, IL-1, IL-6, and TNF-alpha. There was no difference between OLT and control specimens in concentrations of any of the inflammatory variables. There was no difference in MMP-9 levels between groups. Correlation analysis demonstrated a significant positive correlation between patient-reported pain scores and concentrations of IL-1, IL-6, MIP-1 and TNF-alpha.
Conclusion
Intra-articular concentrations of inflammatory cytokines IL-1, IL-6, MIP-1 and TNF-alpha correlated with pain in patients with symptomatic ankle arthritis but were markedly lower in patients with OLTs and asymptomatic control ankles. These cytokines may be involved in the generation of pain with osteoarthritis, but do not appear to be present in high levels with isolated OLTs. These findings may contribute to the development of diagnostic studies to determine the source of ankle pain. It is possible that pain associated with some OLTs may be from a mechanical component rather than a degenerative process as seen in ankle arthritis.