Francois Rannou, MD, PhD
Professor of Medicine
University Paris Descartes, Cochin Hospital, Rehabilitation Department
INSERM U 747, Cartilage Signaling and Pharmacology
Paris, France

Summary of the original abstract

Modification of articular cartilage and subchondral bone pathology in an ovine meniscectomy model of osteoarthritis by avocado and soya unsaponifiables (ASU)
M. A. Cake, R. A. Read, B. Guillou and P. Ghosh
Osteoarthritis and Cartilage 2000, 8:404-411

General Introduction

The 2 main factors involved in the process of human osteoarthritis (OA) are interleukin-1β (IL-1β) and mechanical stress. In previous *in vitro* and *ex vivo* studies, Avocado Soybean Unsaponifiable (ASU) residues have been shown to interact with the molecular signaling pathways of IL-1β and mechanical stress in mouse and human osteoarthritic chondrocytes. Moreover, ASU residues prevent the osteoarthritic osteoblast-induced inhibition of matrix molecule production, which suggests that these compounds may promote cartilage repair by acting on subchondral bone osteoblasts. Taken together, these results suggest a potential structural effect of ASU residues on cartilage *in vivo*. In the present study, the authors used a mechanical stress-dependent animal model of early human OA to examine whether the observed *in vitro* and *ex vivo* protective effects of ASU residues would be found *in vivo*.

Main objective

The main objective of this study is to investigate the effects of an oral preparation of ASU residues in an ovine mechanical stress-dependent model of OA by using computer-assisted histomorphometric methods.

Methods

Forty-eight mature (3-year-old) Merino wethers were used in the experimental protocol. OA was induced surgically by bilateral lateral meniscectomy in 32 animals. The animals were randomly assigned to 2 groups for treatment (n-16 each): meniscectomy plus ASU residues (900 mg/weekday), and meniscectomy plus placebo; 16 animals were non-operated controls. ASU residues and placebo were delivered orally 1 month after the date of the surgical procedure. In each treatment group, animals were killed 3 and 6 months postoperatively, which resulted in 6 groups of 8 animals each. Just after death, joints were immediately dissected and processed for histology. The traditional assessment, gross pathology, was scored to assess cartilage integrity and osteophyte development for precise analysis of 5 joint regions, including medial and lateral femoral condyles (MFC, LFC), medial and lateral tibial plateaux (MTP, LTP), and trochlear groove (TG). These regions were assessed after Toluidine-blue staining as an index of proteoglycan content with use of a modified Mankin's grading system and computer-assisted histomorphometric analysis. Finally, uncalcified cartilage (UCC) and subchondral bone plate (SCP) thickness were determined from Masson's Trichrome-stained sections.

Main results

With the traditional assessment system, gross pathology and histopathological scores did not differ between the ASU-and placebo-treated groups, despite the histopathological score being better, although not significantly, for the ASU-treated group and approaching significance in the LFC compartment at 6 months (P=0.0504). However, computerized image analysis showed significant histological differences between the ASU- and placebo-treated groups mainly at 6 months. At 6 months, the ASU-treated group showed greater Toluidine-blue staining in the MTP, LTP, and TG compartments than did the placebo-treated group (P=0.015, P=0.001, P=0.023, respectively). UCC thickness was higher, although not significantly, in ASU- than placebo-treated group, which was more significant in the middle zone of the LFC and LTP (P=0.0181, P=0.0506, respectively). For the SCP thickness, lateral compartment thickness increased post-meniscectomy but was less in the inner zone of the LTP in the ASU- than placebo-treated group (P=0.033). Finally, the mean body weight was significantly lower in the placebo- than ASU-treated group at 6 months ($P<0.05$).

Strengths of the study

This *in vivo* study is the first to demonstrate a structural effect of ASU by a quantitative method of cartilage and subchondral bone structure. Moreover, this method was previously validated by the authors with a global mean variation of repeated analyses ± 5% and for staining analysis ± 2%. Finally, the results from the present study agree with previous *in vitro* and *ex vivo* studies.

Weaknesses of the study

The weaknesses of the study mainly relate to the absence of a sham-operated animal group and the absence of IL-1 immunostaining in the cartilage and synovial tissue to assess the effect of ASU treatment on the inflammatory process.

Conclusion and perspectives

In an animal model of OA, ASU treatment has a significant positive effect on proteoglycan content along with greater UCC thickness as compared with placebo treatment. Moreover, SCP thickness in the LTP modulated by ASU treatment suggests an effect on subchondral bone. These results suggest a potential disease-modifying activity of ASU residues in OA**.**