

Inhibition of cyclooxygenase 2 expression by diallyl sulfide on joint inflammation induced by urate crystal and IL-1beta

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摘要

Abstract

OBJECTIVE: Investigation of the effects of diallyl sulfide (DAS), a garlic sulfur compound, on joint tissue inflammatory responses induced by monosodium urate (MSU) crystals and interleukin-1beta (IL-1beta). **DESIGN:** The HIG-82 synovial cell line was used to establish the experimental model and DAS regime. Primary cultures of articular chondrocytes and synovial fibroblasts obtained from patients undergoing joint replacement for osteoarthritis were used in experimental studies. Cyclooxygenase (COX) expression following MSU crystal and IL-1beta stimulation with/without DAS co-incubation was assessed by reverse transcription-polymerase chain reaction (RT-PCR), western blotting, and immunocytochemistry and nuclear factor-kappa B (NF-kappaB) activation determined by electrophoretic mobility shift assay. Prostaglandin E2 (PGE(2)) production was measured by enzyme-linked immunosorbent assay (ELISA). DAS effects on COX gene expression in an MSU crystal-induced acute arthritis in rats were assessed by RT-PCR. **RESULTS:** MSU crystals upregulated COX-2 expression in HIG-82 cells and this was inhibited by co-incubation with DAS. DAS inhibited MSU crystal and IL-1beta induced elevation of COX-2 expression in primary synovial cells and chondrocytes. Production of PGE(2) induced by crystals was suppressed by DAS and celecoxib. MSU crystals had no effect on expression of COX-1 in synovial cells. NF-kappaB was activated by MSU crystals and this was blocked by DAS. Increased expression of COX-2 in synovium following intraarticular injection of MSU crystals in a rat model was inhibited by co-administration of DAS. **CONCLUSIONS:** DAS prevents IL-1beta and MSU crystal induced COX-2 upregulation in synovial cells and chondrocytes and ameliorates crystal induced synovitis potentially through a mechanism involving NF-kappaB. Anti-inflammatory actions of DAS may be of value in treatment of joint inflammation.