**INHIBITORY EFFECTS OF METHYLPREDNISOLONE ON ARTICULAR CHONDROCYTE METABOLIC ACTIVITY**

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**Introduction:** The use of intra-articular corticosteroid injections for their anti-inflammatory effects is widespread amongst clinicians. Despite their use in both rheumatoid arthritis and osteoarthritis, the effect of these agents on articular chondrocytes is not fully established. Previous reports suggest a detrimental effect on articular cartilage explants resulting from inhibition of extracellular matrix (ECM) synthesis\(^1\). However, it has also been suggested that the beneficial effects *in vivo* may be due to prevention of inflamed synovium causing articular cartilage degradation\(^2\). Our aim was to assess the *in vitro* effect of a commercially available preparation of methylprednisolone at clinical doses on articular chondrocytes cultured *in vitro*.

**Methods:** Bovine articular chondrocytes were isolated by sequential digestion with pronase and collagenase type IX. Isolated cells were seeded in 2% alginate at 1x10\(^6\) cells.mL\(^{-1}\). The constructs were cultured for up to 15 days in standard culture medium (DMEM + 20% Fetal calf serum) containing varying concentrations of methylprednisolone, including doses equivalent to those found *in vivo*. The medium was replaced every 3 days and representative constructs were removed from culture, digested and assayed for DNA, sulphated glycosaminoglycans (GAG) and hydroxyproline content at time points 0, 3, 6, 9 and 15 days. Further constructs were fixed in 4% paraformaldehyde for standard histology and immunolocalisation of collagen types I, II and chondroitin-6-sulphate. The results were analyzed statistically using an ANOVA test.

**Essential results:** Chondrocytes cultured in methylprednisolone-containing medium showed significant abnormalities in cell morphology compared to controls at day 15. Histologically there was evidence of cell necrosis, and reduced amounts of proteoglycan and collagen type II staining. The effects were dose dependant, with significant damage occurring even at clinical doses (Figure 1). Biochemical analysis revealed a reduction in DNA content (p<0.01) and an inhibition of GAG and collagen synthesis (p<0.05) (Figure 2). In contrast, the control group showed significant amounts of DNA proliferation where the DNA content doubled by day 15. Collagen type II containing ECM synthesis occurred and the chondrocytes maintained their phenotype throughout the culture period.

![Figure 1](image1.png) ![Figure 2](image2.png)

**Discussion:** Methylprednisolone has a significant detrimental effect on cultured articular chondrocytes *in vitro*. There was significant cell necrosis associated with inhibition of ECM synthesis. It is possible that these effects also occur *in vivo*. Therefore, intra-articular corticosteroid injections should be used with extreme caution and further studies *in vivo* should be performed.

**References:**