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Indomethacin and cartilage breakdown

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We have previously shown that indomethacin will accelerate rat femoral head cartilage (FHC) breakdown when implanted subcutaneously in rats in juxtaposition to granulation tissue (De Brito et al 1987; Desa et al 1988). This has recently been confirmed following FHC implantation in mouse air pouches (Bottomley et al 1988) and antigen arthritis in rabbits (Pettipher et al 1988).

We have now shown that indomethacin fails to affect native cartilage in non-inflamed, load bearing joints following daily treatment for 14 days with 1–3 mg kg^{-1} indomethacin orally (control proteoglycan 395 $\mu g \pm 20$ s.e.m; indomethacin treated 405 $\mu g \pm 18$ s.e.m).

To determine the possible effects of mediators, in particular PGE_2, we have now performed some in-vitro experiments in which rat FHC was either cultured with recombinant IL-1α (rIL-1α) or indomethacin. These both failed to lower glycosaminoglycan (GAG) content of the cartilage. However, the level of PGE_2 released into the medium was low in the indomethacin group (0·63 ng mL^{-1}) and high in the rIL-1α group (5·45 ng mL^{-1}).

Table 1. The GAG content of rat femoral head cartilage measured according to Farndale et al (1982) and PGE_2 content of the medium measured by radioimmunoassay according to Salmon (1978). The culture conditions were as described by Desa et al (1988). All assays were performed after 1 week of culture.

Experimental group	n	Proteoglycan estimation (GAG content) μg (mean ± s.e.m.)	PGE_2 concentration ng mL^{-1} (mean ± s.e.m.)
FHC + medium (control)	6	252 ± 13	2·68 ± 0·73
FHC + rIL-1α (1300 units mL^{-1})	6	215 ± 19	5·45 ± 0·33**
FHC + indomethacin (100 μM)	5	214 ± 28	0·633 ± 0·06*
FHC + indomethacin (100 μM) + rIL-1α (1300 units mL)	6	152 ± 11*	0·80 ± 0·04*

*$P < 0·05$. **$P < 0·01$ (Student's t-test)

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When cartilage was cultured with a mixture of rIL-1α plus indomethacin there was a significant loss of GAGs ($P < 0·05$) from the FHC's but a low level of PGE_2 (0·8 ng mL^{-1}) released into the medium. The lack of correlation between PGE_2 and GAG levels would seem to imply that it is unlikely that PGE_2 is involved in the breakdown of cartilage in this system.

In view of our previous findings that exudative inflammation will protect implanted cartilage from breakdown (Sedgwick et al 1985) it is suggested that those often used clinical assessments, of antirheumatics, that depend on heat, redness and swelling, may be misleading. Therefore alleviation of these cardinal signs of acute inflammation which indicate symptomatic relief, may under certain conditions be accelerating the underlying chronic pathological processes.

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