NSAID ADMINISTRATION IN VIVO SUPPRESSES ARTICULAR CARTILAGE METABOLISM

* Bertone, A; * Beluche, L; * Anderson, D; * Rohde, C
+ The Ohio State University College of Veterinary Medicine, Columbus, OH. Orthopedic Research Laboratory, Department of Veterinary Clinical Sciences, 601 Vernon L. Tharp St, Columbus, OH 43210, (614) 292-6661, Fax: (614) 688-5642, bertone.1@osu.edu

Introduction: Phenylbutazone (PBZ) is the most common treatment for joint pain in horses and is a classical NSAID. Sporadic reports of NSAIDs suggest they may suppress articular cartilage metabolism. Our hypotheses were that PBZ administered in vivo for 2 weeks at manufacturer’s recommended dosage would suppress proteoglycan synthesis (PG) and exaggerate chondrocyte inhibition by IL-1β.

Materials and methods: Horses (1-2yr age) were randomly assigned to receive no drug (gp 1; n=5) or PBZ (gp 2; n=6; 4.4 mg/kg orally BID). (Fig.1) Explants were developed from articular cartilage biopsied from the metacarpophalangeal joint at 3 times: before and after 14 days of drug administration, and at euthanasia 2 weeks after drug administration ended. Explants were incubated (72 hours) in standard media or standard media with IL-1β (0.1 ng/ml) and analyzed for articular cartilage proteoglycan synthesis (Na35SO4 incorporation). Media samples were reserved for stromelysin assay. (Fig.2) Quantitative data were analyzed using repeated measures ANOVA and one-way ANOVA for effect of PBZ and IL-1β, respectively. Significance was set at p<0.05.

Results: There was excellent incorporation of Na35SO4 in all horses before drug administration (1.53 +/- 0.19 uCi/g). IL-1β (0.1 ng/ml) significantly inhibited PG synthesis (1.05 +/- 0.09 uCi/g) at time 0 (p=0.03). Systemic PBZ administration significantly decreased proteoglycan synthesis in explants from treated horses (0.88 +/- 0.11 uCi/g; gp 2) compared to untreated horses (1.40 +/- 0.13 uCi/g; gp 1). Further decrease of PG synthesis by IL-1β in gp 2 did not occur (0.96 +/- 0.01 uCi/g). At 30 days there was no difference between groups 1 and 2 in IL-1β challenged explants. (Figs. 3 and 4) No difference was detected for stromelysin levels in II-1β challenged explants compared to control, for grps 1 or 2. (Fig.5)

Conclusion: The systemically administered PBZ, NSAID at 4.4 mg/kg orally BID daily for 14 days significantly decreased PG synthesis in our explant model. As expected, IL-1β depressed chondrocyte metabolism in vitro. Systemic PBZ treatment eliminated inhibition of PG synthesis by this dose of IL-1β (0.1 ng/ml). PG synthesis tended to recover in gp 2 horses 14 days after the last PBZ dose.