NSAIDs in Endotoxemia

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used for treatment of inflammatory disease and in pain management in animals. The potent anti-inflammatory effects of carprofen in animals in combination with minimal renal or enteric adverse effects led these investigators to study alternative therapeutic mechanisms other than cyclooxygenase (COX) inhibition. The objective of this study was to determine if the NSAIDs carprofen, flunixin meglumine, and phenylbutazone have COX-independent effects that specifically inhibit activation of the proinflammatory transcription factor kappa B (NfkB), as does aspirin. The study used assays of purified ovine COX-1 and -2 and cultures of RAW 264.7 murine macrophages. Flunixin meglumine and phenylbutazone were selective inhibitors of COX-1. Carprofen and, to a lesser degree, flunixin meglumine but not phenylbutazone had inhibitory effects on NfkB activation. It seems likely that carprofen and, to a lesser degree, flunixin meglumine can provide a COX-independent-mechanism that can prevent or reduce the deleterious effects of endotoxemia without many of the renal and enteric adverse effects associated with traditional COX inhibitors.

COMMENTARY: Carprofen, flunixin, and phenylbutazone are three of the oldest NSAIDs approved for veterinary use and have been extremely important since their introduction. All NSAIDs have the potential for significant side effects, however; and with more of them being introduced into the marketplace, researchers and practitioners are eager to determine exactly how each compound works. This article demonstrates that we are continuing to find out more about the mechanism of action of these compounds—even older ones, which will help us make better decisions about their risks and benefits to our patients.— Katherine S. Gloyd, DVM